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September 25, 2006

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Confirmation No.: 3322
Art Unit: 1633
Examiner: J.L. Epps Ford

Re: U.S. Patent Application Serial No. 09/199,129 filed November 24, 1998
Inventors: Joseph R. BYRUM *et al.*
Title: Nucleic Acid Molecules and Other Molecules Associated with Plants
Atty. Dkt: 16517.140

Sir:

Transmitted herewith for appropriate action by the U.S. Patent and Trademark Office (PTO) are the following documents:

1. Response to Notice of Non-Compliant Appeal Brief;
2. Appellants' Amended Brief, with attached Claims Appendix (2 pages), Evidence Appendix (1 page), and Related Proceedings Appendix (278 pages); and
3. Return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier.

In the event that extensions of time beyond those petitioned for herewith are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned. Applicants do not believe any additional fees are due in conjunction with this filing. However, if any fees are required in the present application, including any fees for extensions of time, then the Commissioner is hereby authorized to charge such fees to Arnold & Porter LLP Deposit Account No. 50-2387, referencing docket number 16517.140. A duplicate copy of this letter is enclosed.

Sincerely,

Thomas E. Holsten (Reg. No. 46,098)
David R. Marsh (Reg. No. 41,408)

Enclosures



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Joseph R. BYRUM *et al.*

Appln. No.: 09/199,129

Filed: November 24, 1998

For: Nucleic Acid Molecules and Other Molecules Associated with Plants

Conf. No.: 3322

Art Unit: 1633

Examiner: Janet L. Epps Ford

Atty. Docket: 16517.140

Response to Notice of Non-Compliant Appeal Brief

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

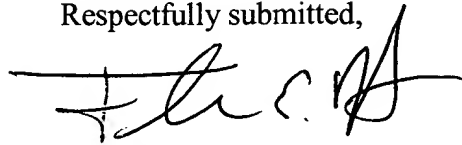
In response to the Notice of Non-Compliant Appeal Brief mailed August 25, 2006, which alleged that Appellants failed to provide a concise explanation of the subject matter defined in each of the independent claims involved in the appeal, referring to the specification by page and line number, Appellants submit herewith an amended copy of the Appellant's Brief filed on October 31, 2005.

It is respectfully submitted that the attached Appellant's Amended Brief is in compliance with 37 C.F.R. § 41.37. The Examiner is encouraged to contact the undersigned should any additional information be necessary.

In the event that extensions of time beyond those petitioned for herewith are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned. Applicants do not believe that any fees in addition to those provided for in the accompanying documents, are due at this time. However, if any fees are required in the present

application, including any fees for extensions of time, authorization to charge such fees is given in the accompanying transmittal letter.

Respectfully submitted,



Thomas E. Holsten (Reg. No. 46,098)

David R. Marsh (Reg. No. 41,408)

Date: September 25, 2006

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of:	Confirmation No.: 3322
Joseph R. BYRUM <i>et al.</i>	Art Unit: 1633
Appln. No.: 09/199,129	Examiner: Janet L. EPPS FORD
Filed: November 24, 1998	Atty. Docket: 16517.140
Title: Nucleic Acid Molecules and Other Molecules Associated with Plants	

APPELLANTS' AMENDED BRIEF

Mail Stop Appeal Brief – Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

This is an Appeal from the Final Rejection of all claims pending in the above-captioned patent application. A Notice of Appeal was filed on August 31, 2005. Authorization to charge the official fees for this filing is given in the accompanying transmittal letter.

1. Real Party in Interest

The real party in interest is Monsanto Company, a Delaware corporation with offices at 800 North Lindbergh Boulevard, St. Louis, Missouri 63167.

2. Related Appeals and Interferences

Appellant identifies the following judicial proceeding, which may have a bearing on the Board's decision in the present Appeal. On May 27, 2004, the Real Party in Interest in the above-captioned matter filed an appeal to the United States Court of Appeals for the Federal Circuit ("Federal Circuit") from a decision by the Board in *In re Fisher*. (U.S. Appln. No. 09/619,643, BPAI Appeal No. 2002-2046, Fed. Cir. Case No. 04-1465). The Federal Circuit's decision in *In re Fisher* may have a bearing on the Board's decision with regard to at least one of the grounds of rejection in the present appeal. A copy of the

Board's decision in Appeal No. 2002-2046, and a copy of *In re Fisher*, 412 F.3d 1365 (Fed. Cir. 2005) are attached hereto in the Related Proceedings Appendix.¹

In addition, Appellant also identifies the following additional Board decisions which may have a bearing on the instant appeal: U.S. Appln. No. 09/654,617, BPAI Appeal No. 2003-1744; U.S. Appln. No. 09/620,392, BPAI Appeal No. 2003-1746; U.S. Appln. No. 09/540,232, BPAI Appeal No. 2003-1137; U.S. Appln. No. 09/440,687, BPAI Appeal No. 2003-1504; U.S. Appln. No. 09/565,240, BPAI Appeal No. 2003-1135; U.S. Appln. No. 09/540,215, BPAI Appeal No. 2003-0996; U.S. Appln. No. 09/552,087, BPAI Appeal No. 2004-1772; and U.S. Appln. No. 09/206,040, BPAI Appeal No. 2002-0078. Copies of the Board's decisions in these Appeals are also attached hereto in the Related Proceedings Appendix.²

Appellant also identifies the following pending appeals before the Board which may have a bearing on the instant appeal: U.S. Appln. No. 09/233,218, BPAI Appeal No. 2004-1725; U.S. Appln. No. 09/540,234, BPAI Appeal No. 2003-1073; U.S. Appln. No. 09/333,535, BPAI Appeal No. 2003-1939; U.S. Appln. No. 09/666,355, BPAI Appeal No. 2004-1034; U.S. Appln. No. 09/552,086, BPAI Appeal No. 2003-1074; U.S. Appln. No. 09/637,086, BPAI Appeal No. 2004-1273; U.S. Appln. No. 09/540,235, BPAI Appeal No. 2004-1275; U.S. Appln. No. 09/553,094, BPAI Appeal No. 2004-1406; U.S. Appln. No. 09/267,199, BPAI Appeal No. 2004-2136; U.S. Appln. No. 09/521,640, BPAI Appeal No. 2004-1666; U.S. Appln. No. 09/371,146, BPAI Appeal No. 2004-1272; U.S. Appln. No. 09/421,106, BPAI Appeal No. 2004-1773; and U.S. Appln. No. 09/732,627, BPAI Appeal No. 2004-1480.³

¹ Copies of the Board's decision in Appeal No. 2002-2046, and a copy of *In re Fisher*, 412 F.3d 1365 (Fed. Cir. 2005) were submitted with Appellants' Brief filed October 31, 2005; however, for the Board's convenience, additional copies are submitted herewith.

² Copies of the Board's decisions in these appeals were submitted with Appellants' Brief filed October 31, 2005; however, for the Board's convenience, additional copies are submitted herewith.

³ At the time Appellant filed Appellants' Brief filed October 31, 2005, it had been requested that these appeals be suspended. Those appeals were subsequently suspended and were withdrawn from the Board of Patent Appeals and Interferences. None of these appeals are currently pending.

3. Status of Claims

Claims 4-12 are pending. Claims 2, 3 and 13-17 were cancelled without prejudice to or disclaimer of the subject matter claimed therein in a amendment filed July 2, 2002. Claim 1 was cancelled without prejudice to or disclaimer of the underlying subject matter in an amendment filed January 26, 2005. Claims 4-12 stand finally rejected under 35 U.S.C. §§101 and 112, first paragraph. Appellant appeals all of the rejections of claims 4-12.

4. Status of Amendments

Appellant has not filed any responses subsequent to Final Rejection in this case.

5. Summary of the Claimed Subject Matter

The claimed subject matter is directed to a transformed plant having a nucleic acid molecule which comprises: (a) an exogenous promoter region which functions in a plant cell to cause the production of an mRNA molecule; (b) a structural nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1 and complement thereof; and (c) a 3' non-translated sequence that functions to cause termination of transcription and addition of polyadenylated ribonucleotides to a 3' end of said mRNA molecule. Specification at page 12, lines 7-15, page 57, line 13 through page 62, line 13, page 19, line 11 through page 24, line 2, and page 62, lines 14-19. The claimed subject matter is also directed to a method of determining a level or pattern in a plant cell or plant tissue of a protein in a plant comprising: (a) incubating, under conditions permitting nucleic acid hybridization, a marker nucleic acid molecule which specifically hybridizes to a nucleic acid molecule having the nucleic acid sequence of SEQ ID NO: 1 or complement thereof, with a complementary nucleic acid molecule obtained from the plant cell or plant tissue, where hybridization permits the detection of an mRNA for the protein; (b) permitting hybridization between said marker nucleic acid molecule and said complementary nucleic acid molecule obtained from said plant cell or plant tissue; and (c) detecting the level or pattern of said complementary nucleic acid, where the detection of said complementary nucleic acid is predictive of the level or pattern of said protein. Specification at page 15, lines 3-16, specification at page 20, line 17 through page 22, line 12, page 33, line 19 through page 34, line 20.

6. Grounds of Rejection to be Reviewed on Appeal

The grounds of rejection to be reviewed in this Appeal are:

(a) pending claims 4-12 stand rejected under 35 U.S.C. § 101, for allegedly not being supported by a specific asserted utility or a well established utility;

(b) pending claims 4-12 stand rejected under 35 U.S.C. § 112, first paragraph for alleged lack of enablement because the claimed invention purportedly lacks utility; and

(c) pending claims 4-12 stand rejected under 35 U.S.C. § 112, first paragraph for alleged insufficiency of written description.

A. Grouping of Claims

Claims 4-12 are pending in this application. All of the claims at issue do not stand or fall together. The separate patentability of claims 4-7 and 8-12 is addressed together in Sections 7.B.(1)(a) and 7.B.(1)(b) below. In addition, the separate patentability of claim 9, and the separate patentability of claim 10 are addressed in Sections 7.B.(1)(c) and 7.B.(1)(d), respectively.

7. Argument

A. Summary of Appellants' Position

As the Supreme Court said in *Brenner v. Manson*, the “basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility ... where specific benefit exists in currently available form.” 383 U.S. 519, 534-35, 148 U.S.P.Q. 689, 695 (1966). Applicants have met their part of the bargain – they have disclosed transformed plants and methods that, in their current form, provide at least one specific benefit to the public, for example, use of the transformed plants in a breeding program. This benefit is specific, and it is a “real world” or substantial benefit. Because the claimed plants and methods provide at least this benefit, they satisfy the utility requirement of 35 U.S.C. § 101. Because the specification teaches how to make and use the claimed plants and methods for the disclosed utilities, the enablement requirement of 35 U.S.C. § 112 has likewise been met.

Furthermore, Applicants have provided an adequate description of the plants and methods that demonstrates Applicants' possession of the claimed invention. Each genus of

nucleic acid molecule in the claimed plants and methods, *e.g.*, transformed plants comprising the nucleic acid molecules comprising a nucleic acid sequence of SEQ ID NO: 1, for example, has been described by the recitation of a common structural feature – the nucleotide sequence of SEQ ID NO: 1 – which distinguishes plants having molecules within the genus from plants having molecules outside of the genus. Because the specification demonstrates that Applicants have possession of (and have provided an adequate description of) the claimed plants and methods, the specification satisfies the written description requirement of 35 U.S.C. § 112.

B. The Claimed Plants and Methods Have Legal Utility

Pending claims 4-12 were erroneously rejected under 35 U.S.C. § 101 because the claimed invention was allegedly “not supported by either a specific and/or substantial utility or a well-established utility.” Final Action at pages 2-6. According to the Final Action, the “specification does not disclose or provide any evidence that points to a specific or substantial biologically significant activity for nucleic acid comprising SEQ ID NO: 1, a plant comprising said nucleic acid, or a method of identifying an unknown protein, such that another non-asserted utility would be well-established.” *Id.* at page 4.

The specification discloses that the claimed transgenic plants and methods can be used in breeding programs and expression assays. *See, e.g.*, Specification at page 18, lines 18-19, page 56, line 15 through page 75, line 10, and page 44, line 20 through page 48, line 21. The Examiner asserts “there is no art of record that discloses or provides any evidence that points to an activity for SEQ ID NO: 1 or its corresponding full length cDNA or the proteins that might be obtained using the full length cDNA to be obtained, such that another non-asserted utility would be well established.” *Id.*

The Examiner further argues that “Applicants have not identified any practical benefit of either the claimed plant or methods since neither the specification as filed, nor any prior art teaches or provides any evidence that defines any beneficial biological activity for the nucleic acid that is transformed into the plant, or assayed for in the claimed methods.” *Id.* at page 5.

This analysis misstates the nature of the asserted uses, ignores disclosed utilities, and misapplies the doctrine of “practical utility” developed by the courts after *Brenner v. Manson*. The “threshold for utility is not high: An invention is ‘useful’ under section 101 if it is capable of providing some identifiable benefit.” *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 1366, 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir. 1999), *citing Brenner v. Manson*, 383 U.S. 519, 534 (1966).

The Federal Circuit has recently reiterated that the “basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived from the public from an invention with *substantial utility*.” *In re Fisher*, 421 F.3d 1365, -- U.S.P.Q.2d -- (Fed. Cir. 2005) (citing *Brenner*, 383 U.S. at 534-35) (emphasis in original). The Court noted that since “*Brenner* our predecessor court, the Court of Customs and Patent Appeals, and this court have required a claimed invention to have a specific and substantial utility to satisfy § 101” *Id.*

Although the Supreme Court has not defined the meaning of the terms “specific” and “substantial”, the Federal Circuit discerned the kind of disclosure an application could contain to establish a specific and substantial utility. *Id.* First, the Court indicated that the specification disclose a utility such that “one skilled in the art can use a claimed discovery in a manner which provides some *immediate benefit to the public*.” *Id.* (emphasis original). Second, the specification should also disclose “a use which is not so vague as to be meaningless,” that is that the claimed invention “can be used to provide a well-defined and particular benefit to the public.” *Id.*

It is well-established that claims must be considered as a whole in determining compliance with § 101. *Diamond v. Diehr*, 450 U.S. 175, 188, 209 U.S.P.Q. 1, 9 (1981). It is inappropriate to dissect claims and consider some elements while ignoring others. *Id.* Further, it is well-established law that “when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown.” *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983).

Appellant has asserted in the specification that the claimed transgenic plants and methods provide clear and immediate benefits, for example, use to follow a plant through a

breeding program (*see, e.g.*, specification at page 18, lines 18-19, page 56, line 15 through page 75, line 10), and to determine the level or pattern of expression of a protein or mRNA associated with that nucleic acid molecule (*see, e.g.*, specification at page 44, line 20 through page 48, line 21). Either of these utilities described alone is enough to satisfy Section 101. Because Applicants need only establish a single utility to satisfy 35 U.S.C. § 101, and have done so in the present case, the premise of the rejection under Section 101 is incorrect, and the rejection should be reversed.

(1) The Claimed Plants and Methods Provide A Specific Benefit, *i.e.*, They Have Specific Utility

The specification describes multiple utilities for the present invention, including in breeding programs and in expression assays. Such uses provide a well-defined use that is not so vague as to be meaningless.

(a) Use of Transgenic Plants in Breeding Programs

For example, one of the utilities disclosed in the specification is use of the claimed transgenic plants in breeding programs (*see, e.g.*, specification at page 18, lines 18-19, page 56, line 15 through page 75, line 10). The Examiner rejects this asserted utility apparently because “neither the specification as filed, nor the prior art teaches or provides any evidence that defines any beneficial biological activity for the nucleic acid.” Final Action at page 5. Contrary to the Examiner’s position, the transformed plants having, *inter alia*, a structural nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO:1 or complement thereof, have utility independent of whether a function is known for the nucleic acid sequence. The specification discloses methods for the preparation of the transgenic plants as well as use in breeding programs to produce plants having genes of interest. *See, e.g.*, specification at page 18, lines 18-19 and page 56, line 15 through page 75, line 10. The specification further describes that the nucleic acid sequences can be used as markers. *See, e.g.*, specification at page 48, line 22 through page 49, line 5. The skilled artisan would recognize that such transformed plants can be more easily followed through a breeding program by the detection of the nucleic acid molecule. These utilities are immediately apparent for the claimed plants and methods without the need for further research.

The Examiner argues that this utility is not specific or substantial, apparently because this utility is “directed to basic research that involves studying the properties of the claimed transformed plant.” Final Action at page 4. The Examiner also argues that this utility is not “specific since the recited use can be generally applied to any plant transformed with any cDNA molecule or fragment thereof.” *Id.* The use of the claimed transformed plants having a nucleic acid molecule comprising, *inter alia*, a structural nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 and complement thereof in plant breeding programs is not a use directed to “basic research.” Rather, using the claimed transformed plants in a breeding program allows the breeder to readily track the transformed plant through the program by identifying progeny plants containing the nucleic acid molecule. Such a use is a well-defined utility. For example, progeny resulting from a cross between a claimed transformed plant having a desired background and a plant having a trait of interest to be introgressed into the transformed plant can be screened quickly for identification of the nucleic acid molecule. Such a plant allows for the high-throughput screening of progeny plants to obtain the desired commercial plant.

The asserted use of the claimed plants in breeding programs is not a “nebulous” or “obscure” expression of utility. The claimed transformed plants have been asserted to work for a specific, *i.e.*, not vague or unknown benefit, for use in breeding programs. This benefit is immediately realized directly from the use of the claimed transformed plants, not from the use of other plants. Such a proven use that provides an acknowledged known benefit to the public satisfies the utility requirement of 35 U.S.C. § 101.

(b) Methods for Determining a Level or Pattern in a Plant Cell or Plant Tissue of a Protein in a Plant

Uses for the claimed methods include detecting the presence or absence or level of expression of the sequence in a sample (*See e.g.*, specification at page 44, line 20 through page 48, line 21). The Examiner suggests that these uses are not legal utilities because “further experimentation would be required to identify the full length cDNA comprising SEQ ID NO: 1, isolate the protein encoded by the full length cDNA, and furthermore identify the biological activity of the encoded protein.” Final Action, at page 6. This is not

correct. Such methods can be used, for example, to assay gene expression in plant cells treated with an herbicide to detect target genes for producing herbicide tolerant plants. The Examiner has not provided any evidence that would reasonably suggest that this cannot be done, and thus has not met the burden of proof required to establish a utility rejection. *See In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995). *Accord In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *In re Langer*, 503 F.2d 1380, 1391, 183 U.S.P.Q. 288, 297 (C.C.P.A. 1974).

One illustrative example of a molecule that can be detected using a claimed method is the nucleic acid sequence of SEQ ID NO: 1. Appellant has specifically disclosed that one use of the claimed method is to detect the level in a plant cell or plant tissue of a protein in a plant. Specification at page 44, line 20 through page 48, line 21. The Examiner denigrates that utility by asserting that it is not specific because it is generally applicable to any nucleic acid. Final Action at pages 4-5. This is not correct. The claimed methods using the nucleic acid molecules are particularly useful, for example, to detect the level in a plant cell or tissue of an mRNA corresponding to SEQ ID NO: 1. *See, e.g.*, specification at page 44, line 20 through page 48, line 21.

In short, the Examiner suggests that the asserted utilities are legally insufficient simply because other molecules can be used for the same purpose, *e.g.*, monitoring gene expression or in a breeding program. That position is wrong as a matter of law – there is no requirement of exclusive utility in the patent law. *See Carl Zeiss Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 U.S.P.Q.2d 1094, 1100 (Fed. Cir. 1991) (“An invention need not be the best or the only way to accomplish a certain result...”). Such an argument would imply that a new golf club has no legal utility because other golf clubs can be used for the same purpose, *i.e.*, hitting golf balls. That position must be rejected as it requires reading “into the patent laws limitations and conditions which the legislature has not expressed,” a practice condemned by the Supreme Court. *See Diamond v. Chakrabarty*, 447 U.S. 303, 308, 206 U.S.P.Q. 193, 196 (1980), *quoting United States v. Dubilier Condenser Corp.*, 289 U.S. 178, 199, 17 U.S.P.Q. 154, 162 (1933).

Moreover, it is factually incorrect that this use is not “specific” to the claimed plants and methods. The claimed methods and plants provide a particularly appropriate and demonstrably useful starting point for example, to screen for compounds with herbicidal activity. A random nucleic acid molecule does not provide an equally good starting point for such an assay as a random nucleic acid molecule would not necessarily correlate to an expressed gene. Furthermore, even if a random nucleic acid molecule provided a better starting point than the claimed nucleic acid molecules, it would not obviate the utility of the claimed plants and methods. An invention may be “less effective than existing devices but nevertheless meet the statutory criteria for patentability.” *Custom Accessories, Inc. v. Jeffrey-Allan Indus.*, 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986).

(c) Methods for Determining a Level or Pattern in a Plant Cell or Tissue of a Protein in a Plant using *In Situ* Hybridization

The specification discloses additional specific and substantial uses of the methods, for example for use in *in situ* hybridizations (*See, e.g.*, Specification at page 45, line 10 through page 47, line 11 and Claim 9). *In situ* hybridization is a highly sensitive technique that can detect as few as 5-10 copies of an RNA sequence per cell and generally involves tissue preparation, hybridization, and washing conditions, and can be used, *inter alia*, to map chromosomal locations of genes, and as diagnostic tools. *See, e.g.*, Specification at page 45, line 10 through page 47, line 11. *In situ* hybridization can be used in a number of uses, for example to determine the spatial population or the steady-state levels of RNA accumulation in a tissue. One of the most common uses of *in situ* hybridization is to localize specific RNA sequences in cells, which is useful for gene mapping, following chromosomes in hybrid lines or detecting chromosomes with translocations, transversions, or deletions. As such, methods for determining the level or pattern in a plant cell or plant tissue of a protein using *in situ* hybridization provides a useful tool for studying cellular processes.

Many of the disclosed utilities in this case, including *in situ* hybridization, are directly analogous to the utilities of a microscope, *i.e.*, the claimed methods employing the recited nucleic acid molecules may be used to locate and measure nucleic acid molecules

within a sample, cell, or organism. The Examiner denigrates such utilities by asserting that these utilities are not “useful” because “[w]ithout identifying the biological activity of the encoded protein, the skilled artisan would not be able to recognize the real-world context of use of the” claimed methods. Final Action, at page 6. However, the fact that, *e.g.*, a new and nonobvious microscope or screening assay can be used for learning about products or processes does not lessen the fact that such “tools” have legal utility. “Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have clear, specific and unquestionable utility (*e.g.*, they are useful in analyzing compounds).” MPEP § 2107.01 at page 2100-33.

Use of the claimed methods to determine the level or pattern of a protein is no more legally insufficient than using a gas chromatograph to analyze the chemical composition of a gas – such use determines information about the gas, not the gas chromatograph. Even if the gas chromatograph detects the absence of a particular chemical element in the gas, that finding does not obviate the utility of the gas chromatograph itself. Information has been obtained about the gas.⁴ Likewise, the claimed methods have utility even if the absence of a particular molecule is detected. Indeed, the absence of the corresponding molecule usefully demonstrates that the nucleic acid molecule is not expressed in a given cell or tissue.

(d) Methods for Determining a Level or Pattern in a Plant Cell or Tissue of a Protein in a Plant using Tissue Printing

The specification also discloses that the methods can be used to detect the level or pattern of a protein using tissue printing (*See*, Claim 10). Tissue printing provides a convenient method to simultaneously screen on a single membrane many tissue sections from different plants or different developmental stages. Tissue printing procedures utilize various films designed to immobilize proteins and nucleic acids. Briefly, a freshly cut section of a plant tissue or organ is pressed gently onto nitrocellulose paper, nylon membrane, or

⁴ For example, gas sampled from crude oil may be analyzed by gas chromatography for the presence or absence of chlorine, which is toxic to catalysts used in gasoline refining even in very low concentrations. The absence of a peak at the molecular weight of chlorine indicates the absence of chlorine in the sample being tested, thereby providing useful information (no chlorine is present, therefore the catalyst will not be destroyed) to the refinery manager. *See, e.g.*, U.S. Patent No. 6,133,740 entitled “Chlorine Specific Gas Chromatographic Detector.”

polyvinylidene difluoride membrane. Such methods can be used to visualize RNA accumulation in tissues and organs and during different developmental stages. The specification discloses that tissue printing can be used for the histochemical localization of various plant enzymes and nucleic acids. *See, e.g.* Specification at page 47, line 12 through page 48, line 17.

Such utility, as are many of the disclosed utilities, is also directly analogous to the utilities of a microscope, *i.e.*, the claimed methods employing the recited nucleic acid molecules in tissue printing may be used to spatially and temporally localize proteins and nucleic acid molecules within a sample, cell, or organism.

The Examiner has failed to provide evidence, or even to suggest a reason for believing that the claimed plants and methods could not be so used. Accordingly, the assertion of this utility in a breeding program or in expression assays satisfies the requirements of 35 U.S.C. § 101. *See In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995).

(2) The Claimed Transgenic Plants and Methods Provide Practical, Real World Benefits, *i.e.*, They Have Substantial Utility

The Final Action also appears to assert that the disclosed uses for the claimed plants or the claimed methods are legally insufficient because they are not “substantial” utilities. Final Action at pages 2-6. The touchstone of “substantial” utility is “real world” or “practical utility.” *See, e.g., Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). “ ‘Practical utility’ is a shorthand way of attributing ‘real world’ value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public.” *Nelson v. Bowler*, 626 F.2d 853, 856, 857, 206 U.S.P.Q. 881, 883 (C.C.P.A. 1980) (“tests evidencing pharmacological activity may manifest a practical utility even though they may not establish a specific therapeutic use”).⁵

⁵ *Accord Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 U.S.P.Q. 739, 747-48 (Fed. Cir. 1985); *Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 1383, 181 U.S.P.Q. 453, 454 (C.C.P.A. 1974).

There can be no question that one skilled in the art can use the claimed transgenic plants and methods in a manner which provides an immediate benefit to the public, for example to easily identify progeny of interest in a breeding program. The detection of transgenic plants provides an immediate benefit to the public because, *e.g.*, it enables a plant breeder to more efficiently allocate resources to progeny plants having a given genetic profile. This information about a plant's genetic profile, like the information about a compound's pharmacological profile in *Nelson*, provides an immediate benefit and thus a practical utility to the public.

(3) The Disclosed Utilities Are Credible to One of Skill in the Art

An assertion of utility must be accepted by the Examiner unless it would not be considered "credible" by a person of ordinary skill in the art. MPEP § 2107 at 2100-29. Cases in which utility was found not to be credible are rare, and usually involve "hare-brained" utilities.⁶ A challenge to the credibility of a utility is essentially a challenge directed to operability, and such a challenge must be supported by a clear statement of "factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability." *In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *see In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995); MPEP § 2107.02 at 2100-41.

Applicants have explicitly identified specific and substantial utilities, not only in the specification, but in Applicants' responses. "To violate [35 U.S.C.] 101 the claimed

⁶ Examples of incredible utilities are given in MPEP § 2107.01 at page 2100-34, and include:

an invention asserted to change the taste of food using a magnetic field (*Fregeau v. Mossinghoff*, 776 F.2d 1034, 227 U.S.P.Q. 848 (Fed. Cir. 1985)), a perpetual motion machine (*Newman v. Quigg*, 877 F.2d 1575, 11 U.S.P.Q. 1340 (Fed. Cir. 1989)), a flying machine operating on "flapping or flutter function" (*In re Houghton*, 433 F.2d 820, 167 U.S.P.Q. 687 (C.C.P.A. 1970)), a method for increasing the energy output of fossil fuels upon combustion through exposure to a magnetic field (*In re Ruskin*, 354 F.2d 395, 148 U.S.P.Q. 221 (C.C.P.A. 1966)), uncharacterized compositions for curing a wide array of cancers (*In re Citron*, 325 F.2d 248, 139 U.S.P.Q. 516 (C.C.P.A. 1963)), a method of controlling the aging process (*In re Eltgroth*, 419 F.2d 918, 164 U.S.P.Q. 221 (C.C.P.A. 1970)), and a method of restoring hair growth (*In re Ferens*, 417 F.2d 1072, 163 U.S.P.Q. 609 (C.C.P.A. 1969)).

device must be totally incapable of achieving a useful result.” *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992). To date, the Examiner has provided no evidence that the claimed plants and methods will not work for the asserted utilities. Unless and until the Examiner can prove that the claimed invention is wholly inoperative, the rejection must be withdrawn.

In view of the above, Applicants contend that the claimed plants and methods are supported by credible, specific, and substantial utilities disclosed in the specification. Moreover, the Examiner has failed to raise any credible evidence challenging the presently asserted utilities. Consequently, the rejection of pending claims 4-12 under 35 U.S.C. §101 is improper and should be reversed.

C. The Claimed Plants and Methods Are Enabled by the Specification

The enablement of the claimed transgenic plants and methods has been challenged. Claims 4-12 have been erroneously rejected as not enabled by the specification, because the claimed nucleic acid molecules allegedly lack utility and therefore cannot be enabled. Final Action at page 7. This rejection is erroneous and has been overcome by the arguments stated above regarding utility because it is well-established law that “the enablement requirement is met if the description enables any mode of making and using the invention.” *Johns Hopkins University v. CellPro*, 152 F.3d 1342, 1361, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998) (emphasis added), *quoting Engel Indus. v. Lockformer Co.*, 946 F.2d 1528, 1533, 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991). Unless and until the Examiner comes forth with evidence to rebut the objective truth of the utilities disclosed in the specification, this enablement rejection must be withdrawn as improper. *See In re Wright*, 999 F.2d 1557, 1561-62, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993); *Ex parte Lemak*, 210 U.S.P.Q. 306, 307 (Bd. App. 1981) (“pure conjecture” does not substantiate rejection for lack of enablement).

D. The Specification Provides An Adequate Written Description of the Claimed Invention

The adequacy of the written description of the claimed invention of claims 4-12 has been challenged by the Examiner because the claimed subject matter was allegedly “not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s)...had possession of the claimed invention.” Final Action at page 7. The Examiner contends that the rejection has been maintained “for the reasons of record set forth in the Examiner’s Answer mailed 10/23/2002.” Final Action at page 7. The Examiner rejects the claims on the basis of “the breadth of the claims are directed to plants transformed with nucleic acids encompassing full length gene sequences (i.e. gene sequences yet to be discovered) and cDNAs comprising SEQ ID NO: 1, sequences that hybridize to SEQ ID NO: 1, and methods which utilize such sequences” Final Action at page 8. However, the specification demonstrates to one skilled in the art that Applicants were in possession of the claimed invention containing the genera of nucleic acid molecules.

(1) The Specification Reflects Applicants’ Possession of the Claimed Invention

The purpose of the written description requirement is to ensure that the inventor had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *Lockwood v. American Airlines*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172, 37 U.S.P.Q.2d 1578, 1581 (Fed. Cir. 1996). If a person of ordinary skill in the art would, after reading the specification, understand that the inventors had possession of the claimed invention, even if not every nuance, then the written description has been met. *In re Alton*, 76 F.3d at 1175, 37 U.S.P.Q.2d at 1584. A person of ordinary skill in the art would, after reading the present specification, understand that Applicants had possession of transgenic plants and methods employing nucleic acid molecules comprising or specifically hybridizing to a nucleic acid sequence of SEQ ID NO: 1. Applicants have provided the nucleotide sequence required by the claims, *e.g.*, SEQ ID NO: 1. Accordingly, Applicants have demonstrated possession of the claimed invention.

The fact that the claims at issue are intended to include molecules that encode the recited enzymes or fragments of the recited nucleic acid sequence, the recited sequence joined with additional sequences, related sequences or complements of the recited

sequence, does not mean that Applicants were any less in possession of the nucleic acid molecules.⁷ It is well-established law that use of the transitional term “comprising” properly leaves the claims “open for the inclusion of unspecified ingredients even in major amounts.” *Ex parte Davis*, 80 U.S.P.Q. 448, 450 (BPAI 1948). *Accord PPG Indus. v. Guardian Indus.*, 156 F.3d 1351, 1354, 48 U.S.P.Q.2d 1351, 1353-54 (Fed. Cir. 1998); *Moleculon Research Corp. v. CBS*, 793 F.2d 1261, 1271, 229 U.S.P.Q. 805, 812 (Fed. Cir. 1986).

The present application describes more than just the nucleotide sequence recited by the claims (*e.g.* SEQ ID NO: 1). For example, the specification describes the transformation of plants with vectors having the claimed nucleic acid molecules (*See, e.g.*, specification at page 66, line 12 through page 75, line 10) as well as methods for determining gene expression (*See, e.g.*, specification at page 15, lines 3-16 and page 47, line 8 through page 50, line 15). Moreover, the present application describes more than just the nucleotide sequence used in the claims (SEQ ID NO: 1). For example, it describes vectors comprising the nucleic acid molecules, Specification at page 56, line 15 through page 66, line 11, and describes how to make the nucleotide sequences and the libraries from which they were originally purified. *See* specification at page 1, line 16 through page 4, line 23, and Examples 1-2.

Moreover, the court determined, in *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1321, 63 U.S.P.Q.2d 1609, 1610 (Fed. Cir. 2002), that the written description inquiry is a factual one determined on a case-by-case basis and that, in a given disclosure, “it may well be that various subsequences, mutations, and mixtures of those sequences are also described to one of skill in the art.” *Enzo*, 296 F.3d at 1326-1327, 63 U.S.P.Q.2d at 1615. Furthermore, it is well established that claims “may be broader than the specific embodiment disclosed in a specification.” *Ralston-Purina Co. v. Far-mor-Co*, 772 F.2d

⁷ If the Examiner is arguing that no possession is shown because the precise claim language is not used in the specification, then it goes beyond what is required by the law. It is well-settled that the description of a claimed invention need not be *in ipso verbis*. *Gentry Gallery v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *In re Alton*, 76 F.3d 1168, 1175, 37 U.S.P.Q.2d 1578, 1583 (Fed. Cir. 1996); *Martin v. Johnson*, 454 F.2d 746, 751, 172 U.S.P.Q. 391, 395 (C.C.P.A. 1972).

1570, 1575, 227 U.S.P.Q. 177, 179 (Fed. Cir. 1985) (*quoting In re Rasmussen*, 650 F.2d 1212, 1215, 211 U.S.P.Q. 323, 326 (C.C.P.A. 1981)). A complete structure of every species within a chemical genus is not required. *See, e.g., Utter v. Hiraga*, 845 F.2d 993, 998, 6 USPQ2d 1709, 1714 (Fed. Cir. 1988) (“A specification may, within the meaning of 35 U.S.C. § 112, ¶ 1, contain a written description of a broadly claimed invention without describing all species that claim encompasses.”).

The Examiner asserts that the claimed invention covers “gene sequences yet to be discovered”, and accordingly Appellant has allegedly not adequately disclosed the genera of nucleic acid molecules. Final Action at page 8. As such, the Examiner appears to require that each nucleic acid molecule within the genera must be described by its complete structure. This requirement is totally unfounded. The Federal Circuit has elucidated a test for written description wherein a genus of nucleic acids may be described by a structural feature that distinguishes members of the claimed genus from non-members of the claimed genus. *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568-69, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997). Applicants have satisfied that test for written description.

In particular, Applicants have disclosed common structural features of the nucleic acid molecule recited in claim 4, for example the nucleotide sequence of SEQ ID NO: 1. The respective common structural feature (the nucleotide sequence of SEQ ID NO: 1) is shared by every nucleic acid molecule in the claimed genera, and it distinguishes the members of the claimed genera from non-members. For example, if a nucleic acid molecule such as an mRNA contains the nucleotide sequence of SEQ ID NO: 1, then it is a member of the genus of nucleic acid molecules comprising a nucleic acid sequence of SEQ ID NO: 1. If a nucleic acid molecule does not contain SEQ ID NO: 1, then it is not a member of that claimed genus. The presence of other nucleotides at either end of the recited sequence will not interfere with the recognition of a claimed nucleic acid molecule as such – it either contains the nucleotides of SEQ ID NO: 1 or it does not. One skilled in the art, after reading the present specification, would clearly know if a nucleic acid molecule contains one of the recited nucleotide sequences. Similarly, if a nucleic acid

molecule specifically hybridizes to the nucleic acid sequence of SEQ ID NO: 1, then it is a member of the genus of nucleic acid molecules recited in claim 8. If the nucleic acid molecule does not specifically hybridize, then it is not a member of that genus.

Thus, claims 4-12 are supported by an adequate written description pursuant to the requirements of 35 U.S.C. § 112, and the rejection should be reversed.

CONCLUSION

In view of the foregoing, it is respectfully requested that the Board of Patent Appeals and Interferences reverse the Rejections and that the subject application be allowed forthwith.

Respectfully submitted,



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CLAIMS APPENDIX

Claims 1-3 (Cancelled)

4. (Previously presented) A transformed plant having a nucleic acid molecule which comprises:
 - (a) an exogenous promoter region which functions in a plant cell to cause the production of an mRNA molecule;
 - (b) a structural nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 and complement thereof; and
 - (c) a 3' non-translated sequence that functions in said plant cell to cause termination of transcription and addition of polyadenylated ribonucleotides to a 3' end of said mRNA molecule.
5. (Previously presented) The transformed plant according to claim 4, wherein said structural nucleic acid molecule is a complement of the nucleic acid sequence of SEQ ID NO: 1.
6. (Original) The transformed plant according to claim 5, wherein said plant is soybean or maize.
7. (Original) The transformed plant according to claim 5, wherein said plant is soybean.
8. (Previously presented) A method for determining a level or pattern in a plant cell or plant tissue of a protein in a plant comprising:

- (a) incubating, under conditions permitting nucleic acid hybridization, a marker nucleic acid molecule, said marker nucleic acid molecule selected from the group of marker nucleic acid molecules which specifically hybridize to a nucleic acid molecule having the nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 or complement thereof, with a complementary nucleic acid molecule obtained from said plant cell or plant tissue, wherein nucleic acid hybridization between said marker nucleic acid molecule and said complementary nucleic acid molecule obtained from said plant cell or plant tissue permits the detection of an mRNA for said protein;
 - (b) permitting hybridization between said marker nucleic acid molecule and said complementary nucleic acid molecule obtained from said plant cell or plant tissue; and
 - (c) detecting the level or pattern of said complementary nucleic acid, wherein the detection of said complementary nucleic acid is predictive of the level or pattern of said protein.
9. (Original) The method of claim 8, wherein said level or pattern is detected by *in situ* hybridization.
10. (Original) The method of claim 8, wherein said level or pattern is detected by tissue printing.
11. (Original) The method of claim 8, wherein said plant is maize or soybean.
12. (Original) The method of claim 11, wherein said plant is soybean.

Claims 13-17 (Cancelled)

EVIDENCE APPENDIX

No New Evidence

RELATED PROCEEDINGS APPENDIX

Attached are copies of Decisions on Appeal that issued in the following applications:

1. *In re Fisher*, 412 F.3d 1365 (Fed. Cir. 2005)
2. U.S. Appln. No. 09/619,643, BPAI Appeal No. 2002-2046
3. U.S. Appln. No. 09/654,617, BPAI Appeal No. 2003-1744
4. U.S. Appln. No. 09/620,392, BPAI Appeal No. 2003-1746
5. U.S. Appln. No. 09/540,232, BPAI Appeal No. 2003-1137
6. U.S. Appln. No. 09/440,687, BPAI Appeal No. 2003-1504
7. U.S. Appln. No. 09/565,240, BPAI Appeal No. 2003-1135
8. U.S. Appln. No. 09/540,215, BPAI Appeal No. 2003-0996
9. U.S. Appln. No. 09/552,087, BPAI Appeal No. 2004-1772
10. U.S. Appln. No. 09/206,040, BPAI Appeal No. 2002-0078



United States Court of Appeals for the Federal Circuit

04-1465
(Serial No. 09/619,643)

IN RE DANE K. FISHER and RAGHUNATH V. LALGUDI

Seth P. Waxman, Wilmer Cutler Pickering Hale and Dorr LLP, of Washington, DC, argued for appellants. With him on the brief were William F. Lee and Richard W. O'Neill, of Boston, Massachusetts; and William G. McElwain and Henry N. Wixon, of Washington, DC.

Stephen Walsh, Associate Solicitor, United States Patent and Trademark Office, of Arlington, Virginia, argued for the Director of the Patent and Trademark Office. With him on the brief were John M. Whealan, Solicitor, and Thomas W. Krause, Associate Solicitor.

Joseph A. Keyes, Jr., of Washington, DC, for amicus curiae Association of American Medical Colleges.

Marc S. Gold, of Washington, DC, for amicus curiae National Academy of Sciences.

Donald R. Stuart, of Indianapolis, Indiana, for amicus curiae Dow AgroSciences LLC. With him on the brief was Kenneth B. Ludwig.

Paula K. Davis, of Indianapolis, Indiana, for amicus curiae Eli Lilly and Company. With her on the brief were Steven P. Caltrider and James J. Kelley.

Michael C. Schiffer, of Irvine, California, for amicus curiae Baxter Healthcare Corporation.

Darrel C. Karl, Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P., of Washington, DC, for amicus curiae American College of Medical Genetics.

Jeffrey P. Kushan, Sidley Austin Brown & Wood, LLP, of Washington, DC, for amicus curiae Genentech, Inc. With him on the brief were Kathi A. Cover and David L. Fitzgerald.

George C. Yu, of Emeryville, California, for amicus curiae Affymetrix, Inc.

Appealed from: United States Patent and Trademark Office
Board of Patent Appeals and Interferences

United States Court of Appeals for the Federal Circuit

04-1465
(Serial No. 09/619,643)

IN RE DANE K. FISHER and RAGHUNATH V. LALGUDI,

DECIDED: September 7, 2005

Before MICHEL, Chief Judge, RADER and BRYSON, Circuit Judges.

Opinion for the court filed by Chief Judge MICHEL. Dissenting opinion filed by Circuit Judge RADER.

MICHEL, Chief Judge.

Dane K. Fisher and Raghunath Lalgudi (collectively “Fisher”)¹ appeal from the decision of the U.S. Patent and Trademark Office (“PTO”) Board of Patent Appeals and Interferences (“Board”) affirming the examiner’s final rejection of the only pending claim of application Serial No. 09/619,643 (the “643 application”), entitled “Nucleic Acid Molecules and Other Molecules Associated with Plants,” as unpatentable for lack of utility under 35 U.S.C. § 101 and lack of enablement under 35 U.S.C. § 112, first paragraph. Ex parte Fisher, App. No. 2002-2046 (Bd. Pat. App. Int. Mar. 16, 2004) (“Board Decision”). This appeal was submitted after oral argument on May 3, 2005. Because we conclude that substantial evidence supports the Board’s findings that the

¹ The real party in interest is Monsanto Technology LLC, which is owned by the Monsanto Company.

claimed invention lacks a specific and substantial utility and that the '643 application does not enable one of ordinary skill in the art to use the invention, we affirm.

I. BACKGROUND

A. Molecular Genetics and ESTs

The claimed invention relates to five purified nucleic acid sequences that encode proteins and protein fragments in maize plants. The claimed sequences are commonly referred to as "expressed sequence tags" or "ESTs." Before delving into the specifics of this case, it is important to understand more about the basic principles of molecular genetics and the role of ESTs.

Genes are located on chromosomes in the nucleus of a cell and are made of deoxyribonucleic acid ("DNA"). DNA is composed of two strands of nucleotides in double helix formation. The nucleotides contain one of four bases, adenine ("A"), guanine ("G"), cytosine ("C"), and thymine ("T"), that are linked by hydrogen bonds to form complementary base pairs (i.e., A-T and G-C).

When a gene is expressed in a cell, the relevant double-stranded DNA sequence is transcribed into a single strand of messenger ribonucleic acid ("mRNA"). Messenger RNA contains three of the same bases as DNA (A, G, and C), but contains uracil ("U") instead of thymine. mRNA is released from the nucleus of a cell and used by ribosomes found in the cytoplasm to produce proteins.

Complementary DNA ("cDNA") is produced synthetically by reverse transcribing mRNA. cDNA, like naturally occurring DNA, is composed of nucleotides containing the four nitrogenous bases, A, T, G, and C. Scientists routinely compile cDNA into libraries to study the kinds of genes expressed in a certain tissue at a particular point in time.

One of the goals of this research is to learn what genes and downstream proteins are expressed in a cell so as to regulate gene expression and control protein synthesis.²

An EST is a short nucleotide sequence that represents a fragment of a cDNA clone. It is typically generated by isolating a cDNA clone and sequencing a small number of nucleotides located at the end of one of the two cDNA strands. When an EST is introduced into a sample containing a mixture of DNA, the EST may hybridize with a portion of DNA. Such binding shows that the gene corresponding to the EST was being expressed at the time of mRNA extraction.

Claim 1 of the '643 application recites:

A substantially purified nucleic acid molecule that encodes a maize protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 5.

The ESTs set forth in SEQ ID NO: 1 through SEQ ID NO: 5 are obtained from cDNA library LIB3115, which was generated from pooled leaf tissue harvested from maize plants (RX601, Asgrow Seed Company, Des Moines, Iowa, U.S.A.) grown in the fields at Asgrow research stations. SEQ ID NO:1 through SEQ ID NO:5 consist of 429, 423, 365, 411, and 331 nucleotides, respectively. When Fisher filed the '643 application, he claimed ESTs corresponding to genes expressed from the maize pooled leaf tissue at the time of anthesis. Nevertheless, Fisher did not know the precise structure or function of either the genes or the proteins encoded for by those genes.

The '643 application generally discloses that the five claimed ESTs may be used in a variety of ways, including: (1) serving as a molecular marker for mapping the entire

² We have discussed the basic principles of molecular genetics more extensively in prior cases. See, e.g., In re Deuel, 51 F.3d 1552, 1554-56 (Fed. Cir. 1995); Amgen, Inc. v. Chugai Pharm. Co., Ltd., 927 F.2d 1200, 1207-08 (Fed. Cir. 1991); In re O'Farrell, 853 F.2d 894, 895-99 (Fed. Cir. 1988).

maize genome, which consists of ten chromosomes that collectively encompass roughly 50,000 genes; (2) measuring the level of mRNA in a tissue sample via microarray technology to provide information about gene expression; (3) providing a source for primers for use in the polymerase chain reaction ("PCR") process to enable rapid and inexpensive duplication of specific genes; (4) identifying the presence or absence of a polymorphism; (5) isolating promoters via chromosome walking; (6) controlling protein expression; and (7) locating genetic molecules of other plants and organisms.

B. Final Rejection

In a final rejection, dated September 6, 2001, the examiner rejected claim 1 for lack of utility under § 101. The examiner found that the claimed ESTs were not supported by a specific and substantial utility. She concluded that the disclosed uses were not specific to the claimed ESTs, but instead were generally applicable to any EST. For example, the examiner noted that any EST may serve as a molecular tag to isolate genetic regions. She also concluded that the claimed ESTs lacked a substantial utility because there was no known use for the proteins produced as final products resulting from processes involving the claimed ESTs. The examiner stated: "Utilities that require or constitute carrying out further research to identify or reasonably confirm a 'real world' context of use are not substantial utilities."

The examiner also rejected the claimed application for lack of enablement under § 112, first paragraph. She reasoned that one skilled in the art would not know how to use the claimed ESTs because the '643 application did not disclose a specific and substantial utility for them.

On July 19, 2000, Fisher filed a notice of appeal with the Board.

C. Board Proceedings

The Board considered each of Fisher's seven potential uses but noted that Fisher focused its appeal on only two: (1) use for the identification of polymorphisms; and (2) use as probes or as a source for primers. As to the first, the Board found that the application failed to explain why the claimed ESTs would be useful in detecting polymorphisms in maize plants. Board Decision, slip op. at 14. The Board reasoned that "[w]ithout knowing any further information in regard to the gene represented by an EST, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage." Id., slip op. at 15. Thus, the Board concluded that Fisher's asserted uses for the claimed ESTs tended to the "insubstantial use" end of the spectrum between a substantial and an insubstantial utility. Id.

The Board also concluded that using the claimed ESTs to isolate nucleic acid molecules of other plants and organisms, which themselves had no known utility, is not a substantial utility. Id., slip op. at 16. Specifically, the Board noted that Fisher argued that the "claimed ESTs may be useful in searching for promoters that are only active in leaves at the time of anthesis." Id. The Board found, however, that the application failed to show that the claimed ESTs would be expressed only during anthesis or that they would be capable of isolating a promoter active in maize leaves at the time of anthesis. Id., slip op. at 18.

Additionally, the Board addressed the remaining asserted utilities, highlighting in particular the use of the claimed ESTs to monitor gene expression by measuring the level of mRNA through microarray technology and to serve as molecular markers. The Board found that using the claimed ESTs in screens does not provide a specific benefit

because the application fails to provide any teaching regarding how to use the data relating to gene expression. Id., slip op. at 21. The Board analogized the facts to those in Brenner v. Manson, 383 U.S. 519 (1966), in which an applicant claimed a process of making a compound having no known use. In that case, the Supreme Court affirmed the rejection of the application on § 101 grounds. Here, the Board reasoned: “Just as the process in Brenner lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, because even if used in gene expression assays, the specification does not disclose how to use SEQ ID NO: 1-5 specific gene expression data.” Id., slip op. at 22. The Board offered a similar rationale for the use of the claimed ESTs as molecular markers. Id., slip op. at 24. Accordingly, the Board affirmed the examiner’s rejection of the ’643 application for lack of utility under § 101. The Board also affirmed the examiner’s rejection of the ’643 application for lack of enablement under § 112, first paragraph, since the enablement rejection was made as a corollary to the utility rejection.

Fisher timely appealed. We have jurisdiction over this appeal pursuant to 28 U.S.C. § 1295(a)(4) and 35 U.S.C. §§ 141 and 144.

II. DISCUSSION

Whether an application discloses a utility for a claimed invention is a question of fact. In re Ziegler, 992 F.2d 1197, 1200 (Fed. Cir. 1993). We consequently review the Board’s determination that the ’643 application failed to satisfy the utility requirement of § 101 for substantial evidence. In re Gartside, 203 F.3d 1305, 1315 (Fed. Cir. 2000) (“Because our review of the Board’s decision is confined to the factual record compiled

by the Board, we accordingly conclude that the 'substantial evidence' standard is appropriate for our review of Board factfindings.").

A. Utility

1.

Fisher asserts that the Board unilaterally applied a heightened standard for utility in the case of ESTs, conditioning patentability upon "some undefined 'spectrum' of knowledge concerning the corresponding gene function." Fisher contends that the standard is not so high and that Congress intended the language of § 101 to be given broad construction. In particular, Fisher contends that § 101 requires only that the claimed invention "not be frivolous, or injurious to the well-being, good policy, or good morals of society," essentially adopting Justice Story's view of a useful invention from Lowell v. Lewis, 15 F. Cas. 1018, 1019 (No. 8568) (C.C. Mass. 1817). Under the correct application of the law, Fisher argues, the record shows that the claimed ESTs provide seven specific and substantial uses, regardless whether the functions of the genes corresponding to the claimed ESTs are known. Fisher claims that the Board's attempt to equate the claimed ESTs with the chemical compositions in Brenner was misplaced and that several decisions in the field of pharmaceuticals, namely, Cross v. Iizuka, 753 F.2d 1040 (Fed. Cir. 1985), Nelson v. Bowler, 626 F.2d 853 (C.C.P.A. 1980), and In re Jolles, 628 F.2d 1322 (C.C.P.A. 1980), are analogous and support finding utility of the claimed ESTs. Fisher likewise argues that the general commercial success of ESTs in the marketplace confirms the utility of the claimed ESTs. Hence, Fisher avers that the Board's decision was not supported by substantial evidence and should be reversed.

The government agrees with Fisher that the utility threshold is not high, but disagrees with Fisher's allegation that the Board applied a heightened utility standard. The government contends that a patent applicant need disclose only a single specific and substantial utility pursuant to Brenner, the very standard articulated in the PTO's "Utility Examination Guidelines" ("Utility Guidelines") and followed here when examining the '643 application. It argues that Fisher failed to meet that standard because Fisher's alleged uses are so general as to be meaningless. What is more, the government asserts that the same generic uses could apply not only to the five claimed ESTs but also to any EST derived from any organism. It thus argues that the seven utilities alleged by Fisher are merely starting points for further research, not the end point of any research effort. It further disputes the importance of the commercial success of ESTs in the marketplace, pointing out that Fisher's evidence involved only databases, clone sets, and microarrays, not the five claimed ESTs. Therefore, the government contends that we should affirm the Board's decision.

Several academic institutions and biotechnology and pharmaceutical companies³ write as amici curiae in support of the government. Like the government, they assert that Fisher's claimed uses are nothing more than a "laundry list" of research plans, each general and speculative, none providing a specific and substantial benefit in currently available form. The amici also advocate that the claimed ESTs are the objects of further research aimed at identifying what genes of unknown function are expressed during anthesis and what proteins of unknown function are encoded for by those genes.

³ Amici in support of the government include Affymetrix, Inc., American College of Medical Genetics, Association of American Medical Colleges, Baxter Healthcare Corporation, Dow AgroSciences LLC, Eli Lilly and Company, Genentech, Inc., National Academy of Sciences, and the University of North Carolina School of Law.

Until the corresponding genes and proteins have a known function, the amici argue, the claimed ESTs lack utility under § 101 and are not patentable.

We agree with both the government and the amici that none of Fisher's seven asserted uses meets the utility requirement of § 101. Section 101 provides: "Whoever invents . . . any new and useful . . . composition of matter . . . may obtain a patent therefor" (Emphasis added). In Brenner, the Supreme Court explained what is required to establish the usefulness of a new invention, noting at the outset that "a simple, everyday word ["useful," as found in § 101] can be pregnant with ambiguity when applied to the facts of life." 383 U.S. at 529. Contrary to Fisher's argument that § 101 only requires an invention that is not "frivolous, injurious to the well-being, good policy, or good morals of society," the Supreme Court appeared to reject Justice Story's de minimis view of utility. Id. at 532-33 (citation omitted). The Supreme Court observed that Justice Story's definition "sheds little light on our subject," on the one hand framing the relevant inquiry as "whether the invention in question is 'frivolous and insignificant'" if narrowly read, while on the other hand "allowing the patenting of any invention not positively harmful to society" if more broadly read. Id. at 533. In its place, the Supreme Court announced a more rigorous test, stating:

The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point – where specific benefit exists in currently available form – there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

Brenner, 383 U.S. at 534-35 (emphases added). Following Brenner, our predecessor court, the Court of Customs and Patent Appeals, and this court have required a claimed invention to have a specific and substantial utility to satisfy § 101. See, e.g., Fujikawa v.

Wattanasin, 93 F.3d 1559, 1563 (Fed. Cir. 1996) (“Consequently, it is well established that a patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed.”).

The Supreme Court has not defined what the terms “specific” and “substantial” mean per se. Nevertheless, together with the Court of Customs and Patent Appeals, we have offered guidance as to the uses which would meet the utility standard of § 101. From this, we can discern the kind of disclosure an application must contain to establish a specific and substantial utility for the claimed invention.

Courts have used the labels “practical utility” and “real world” utility interchangeably in determining whether an invention offers a “substantial” utility. Indeed, the Court of Customs and Patent Appeals stated that “[p]ractical utility” is a shorthand way of attributing ‘real-world’ value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public.” Nelson, 626 F.2d at 856 (emphasis added).⁴ It thus is clear that an application must show that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research. Simply put, to satisfy the “substantial” utility requirement, an asserted use must show that that claimed invention has a significant and presently available benefit to the public.

Turning to the “specific” utility requirement, an application must disclose a use which is not so vague as to be meaningless. Indeed, one of our predecessor courts has observed “that the nebulous expressions ‘biological activity’ or ‘biological properties’

⁴ In Cross, this court considered the phrase “practical utility” to be synonymous with the phrase “substantial utility.” 753 F.2d at 1047, n.13.

appearing in the specification convey no more explicit indication of the usefulness of the compounds and how to use them than did the equally obscure expression 'useful for technical and pharmaceutical purposes' unsuccessfully relied upon by the appellant in In re Diedrich." In re Kirk, 376 F.2d 936, 941 (C.C.P.A. 1967). Thus, in addition to providing a "substantial" utility, an asserted use must also show that that claimed invention can be used to provide a well-defined and particular benefit to the public.

In 2001, partially in response to questions about the patentability of ESTs, the PTO issued Utility Guidelines governing its internal practice for determining whether a claimed invention satisfies § 101. See Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001). The PTO incorporated these guidelines into the Manual of Patent Examining Procedure ("MPEP"). See U.S. Pat. & Trademark Off., Manual of Patent Examining Procedure § 2107 (8th ed. 2001, rev. May 2004). The MPEP and Guidelines "are not binding on this court, but may be given judicial notice to the extent they do not conflict with the statute." Enzo Biochem v. Gen-Probe, 323 F.3d 956, 964 (Fed. Cir. 2002) (citing Molins PLC v. Textron, Inc., 48 F.3d 1172, 1180 n.10 (Fed. Cir. 1995)). According to the Utility Guidelines, a specific utility is particular to the subject matter claimed and would not be applicable to a broad class of invention. Manual of Patent Examining Procedure § 2107.01. The Utility Guidelines also explain that a substantial utility defines a "real world" use. In particular, "[u]tilities that require or constitute carrying out further research to identify or reasonably confirm a 'real world' context of use are not substantial utilities." Id. Further, the Utility Guidelines discuss "research tools," a term often given to inventions used to conduct research. The PTO particularly cautions that

[a]n assessment that focuses on whether an invention is useful only in a research setting thus does not address whether the invention is in fact “useful” in a patent sense. [The PTO] must distinguish between inventions that have a specifically identified substantial utility and inventions whose asserted utility requires further research to identify or reasonably confirm.

Id. The PTO’s standards for assessing whether a claimed invention has a specific and substantial utility comport with this court’s interpretation of the utility requirement of § 101.

Turning to the parties’ arguments, Fisher first raises a legal issue, charging that the Board applied a heightened standard for utility in the case of ESTs. Fisher apparently bases this argument on statements made by the Board in connection with its discussion of whether the claimed ESTs can be used to identify a polymorphism. In that context, the Board stated:

Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the gene and its role in the plant’s development lies the line between ‘utility’ and ‘substantial utility.’ We need not draw the line or further define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.

Board Decision, slip op. at 15 (emphasis added). Fisher reads the word “spectrum” out of context, claiming that the word somehow implies the application of a higher standard for utility than required by § 101. We conclude, however, that the Board did not apply an incorrect legal standard. In its decision, the Board made reference to a “spectrum” to differentiate between a substantial utility, which satisfies the utility requirement of § 101, and an insubstantial utility, which fails to satisfy § 101. The Board plainly did not announce or apply a new test for assessing the utility of ESTs. It simply followed the Utility Guidelines and MPEP, which mandate the specific and substantial utility test set forth in Brenner. Indeed, we note that Example 9 of the PTO’s “Revised Interim Utility

Guidelines Training Materials” is applicable to the facts here. See U.S. Pat. & Trademark Off., Revised Interim Utility Guidelines Training Materials 50-53 (1999), available at www.uspto.gov/web/menu/utility.pdf. In that example, a cDNA fragment disclosed as being useful as a probe to obtain the full length gene corresponding to a cDNA fragment was deemed to lack a specific and substantial utility. Additionally, the MPEP particularly explains that a claim directed to a polynucleotide disclosed to be useful as a “gene probe” or “chromosome marker,” as is the case here, fails to satisfy the specific utility requirement unless a specific DNA target is also disclosed. Manual of Patent Examining Procedure § 2107.01.

Regarding the seven uses asserted by Fisher, we observe that each claimed EST uniquely corresponds to the single gene from which it was transcribed (“underlying gene”). As of the filing date of the '643 application, Fisher admits that the underlying genes have no known functions. Fisher, nevertheless, claims that this fact is irrelevant because the seven asserted uses are not related to the functions of the underlying genes. We are not convinced by this contention. Essentially, the claimed ESTs act as no more than research intermediates that may help scientists to isolate the particular underlying protein-encoding genes and conduct further experimentation on those genes. The overall goal of such experimentation is presumably to understand the maize genome – the functions of the underlying genes, the identity of the encoded proteins, the role those proteins play during anthesis, whether polymorphisms exist, the identity of promoters that trigger protein expression, whether protein expression may be controlled, etc. Accordingly, the claimed ESTs are, in words of the Supreme Court, mere “object[s] of use-testing,” to wit, objects upon which scientific research could be

performed with no assurance that anything useful will be discovered in the end.
Brenner, 383 U.S. at 535.

Fisher compares the claimed ESTs to certain other patentable research tools, such as a microscope. Although this comparison may, on first blush, be appealing in that both a microscope and one of the claimed ESTs can be used to generate scientific data about a sample having unknown properties, Fisher's analogy is flawed. As the government points out, a microscope has the specific benefit of optically magnifying an object to immediately reveal its structure. One of the claimed ESTs, by contrast, can only be used to detect the presence of genetic material having the same structure as the EST itself. It is unable to provide any information about the overall structure let alone the function of the underlying gene. Accordingly, while a microscope can offer an immediate, real world benefit in a variety of applications, the same cannot be said for the claimed ESTs. Fisher's proposed analogy is thus inapt. Hence, we conclude that Fisher's asserted uses are insufficient to meet the standard for a "substantial" utility under § 101.

Moreover, all of Fisher's asserted uses represent merely hypothetical possibilities, objectives which the claimed ESTs, or any EST for that matter, could possibly achieve, but none for which they have been used in the real world. Focusing on the two uses emphasized by Fisher at oral argument, Fisher maintains that the claimed ESTs could be used to identify polymorphisms or to isolate promoters. Nevertheless, in the face of a utility rejection, Fisher has not presented any evidence, as the Board well noted, showing that the claimed ESTs have been used in either way. That is, Fisher does not present either a single polymorphism or a single promoter,

assuming at least one of each exists, actually identified by using the claimed ESTs. Further, Fisher has not shown that a polymorphism or promoter so identified would have a “specific and substantial” use. The Board, in fact, correctly recognized this very deficiency and cited it as one of the reasons for upholding the examiner’s final rejection.

With respect to the remaining asserted uses, there is no disclosure in the specification showing that any of the claimed ESTs were used as a molecular marker on a map of the maize genome. There also is no disclosure establishing that any of the claimed ESTs were used or, for that matter, could be used to control or provide information about gene expression. Significantly, despite the fact that maize leaves produce over two thousand different proteins during anthesis, Fisher failed to show that one of the claimed ESTs translates into a portion of one of those proteins. Fisher likewise did not provide any evidence showing that the claimed ESTs were used to locate genetic molecules in other plants and organisms. What is more, Fisher has not proffered any evidence showing that any such generic molecules would themselves have a specific and substantial utility. Consequently, because Fisher failed to prove that its claimed ESTs can be successfully used in the seven ways disclosed in the '643 application, we have no choice but to conclude that the claimed ESTs do not have a “substantial” utility under § 101.

Furthermore, Fisher’s seven asserted uses are plainly not “specific.” Any EST transcribed from any gene in the maize genome has the potential to perform any one of the alleged uses. That is, any EST transcribed from any gene in the maize genome may be a molecular marker or a source for primers. Likewise, any EST transcribed from any gene in the maize genome may be used to measure the level of mRNA in a

tissue sample, identify the presence or absence of a polymorphism, isolate promoters, control protein expression, or locate genetic molecules of other plants and organisms. Nothing about Fisher's seven alleged uses set the five claimed ESTs apart from the more than 32,000 ESTs disclosed in the '643 application or indeed from any EST derived from any organism. Accordingly, we conclude that Fisher has only disclosed general uses for its claimed ESTs, not specific ones that satisfy § 101.

We agree with the Board that the facts here are similar to those in Brenner. There, as noted above, the applicant claimed a process for preparing compounds of unknown use. Similarly, Fisher filed an application claiming five particular ESTs which are capable of hybridizing with underlying genes of unknown function found in the maize genome. The Brenner court held that the claimed process lacked a utility because it could be used only to produce a compound of unknown use. The Brenner court stated: "We find absolutely no warrant for the proposition that although Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing, a different set of rules was meant to apply to the process which yielded the unpatentable product." 383 U.S. at 535. Applying that same logic here, we conclude that the claimed ESTs, which do not correlate to an underlying gene of known function, fail to meet the standard for utility intended by Congress.

In addition to approving of the Board's reliance on Brenner, we observe that the facts here are even more analogous to those presented in Kirk, 376 F.2d 936, and In re Joly, 376 F.2d 906 (C.C.P.A. 1967), two cases decided by our predecessor court shortly after Brenner. In Kirk, the applicant sought to patent new steroidal compounds

disclosed as having two possible utilities. First, the applicant alleged that the claimed compounds were useful for their “biological activity” because “one skilled in the art would know how to use the compounds . . . to take advantage of their presently-existing biological activity.” Kirk, 376 F.2d at 939. The court rejected this claimed utility on the ground that it was not sufficiently “specific,” but was instead “nebulous.” Id. at 941.

Second, the applicant asserted that the claimed compounds could be used by skilled chemists as intermediates in the preparation of final steroidal compounds of unknown use. Relying on Brenner, the court reasoned:

It seems clear that, if a process for producing a product of only conjectural use is not itself “useful” within § 101, it cannot be said that the starting materials for such a process – i.e., the presently claimed intermediates – are “useful.” It is not enough that the specification disclose that the intermediate exists and that it “works,” reacts, or can be used to produce some intended product of no known use. Nor is it enough that the product disclosed to be obtained from the intermediate belongs to some class of compounds which now is, or in the future might be, the subject of research to determine some specific use. Cf. Reiners v. Mehlretter, 236 F.2d 418, 421 [(C.C.P.A. 1956)] where compounds employed as intermediates to produce other directly useful compounds were found to be themselves useful.

Id. at 945-46 (emphasis added). Therefore, the court affirmed the Board’s rejection of the claimed compounds for lack of utility.

The facts in Joly are nearly identical to the facts in Kirk. The Joly applicant filed an application claiming compounds useful as intermediates in preparing steroids that were themselves not shown or known to be useful, but that were similar in chemical structure to steroids of known pharmacological usefulness. The court adopted the reasoning of the Kirk court in its entirety and affirmed the Board’s decision rejecting the claimed intermediates for failing to comply with § 101. Joly, 376 F.2d at 908-09.

Just as the claimed compounds in Kirk and Joly were useful only as intermediates in the synthesis of other compounds of unknown use, the claimed ESTs can only be used as research intermediates in the identification of underlying protein-encoding genes of unknown function. The rationale of Kirk and Joly thus applies here. In the words of the Kirk court:

We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.

376 F.2d at 942 (emphasis added).

That the Kirk and Joly decisions involved chemical compounds, while the present case involves biological entities, does not distinguish these decisions. The rationale presented therein, having been drawn from principles set forth by the Supreme Court in Brenner, applies with equal force in the fields of chemistry and biology as well as in any scientific discipline. In Brenner, the Supreme Court was primarily concerned with creating an unwarranted monopoly to the detriment of the public:

Whatever weight is attached to the value of encouraging disclosure and of inhibiting secrecy, we believe a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development, without compensating benefit to the public. . . . This is not to say that we mean to disparage the importance of contributions to the fund of scientific information short of the invention of something "useful," or that we are blind to the prospect that what now

seems without “use” may tomorrow command the grateful attention of the public. But a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. [A] patent system must be related to the world of commerce rather than to the realm of philosophy.

Brenner, 383 U.S. at 535-36 (citations, quotation, and footnote omitted). Here, granting a patent to Fisher for its five claimed ESTs would amount to a hunting license because the claimed ESTs can be used only to gain further information about the underlying genes and the proteins encoded for by those genes. The claimed ESTs themselves are not an end of Fisher’s research effort, but only tools to be used along the way in the search for a practical utility. Thus, while Fisher’s claimed ESTs may add a noteworthy contribution to biotechnology research, our precedent dictates that the ’643 application does not meet the utility requirement of § 101 because Fisher does not identify the function for the underlying protein-encoding genes. Absent such identification, we hold that the claimed ESTs have not been researched and understood to the point of providing an immediate, well-defined, real world benefit to the public meriting the grant of a patent.

2.

Fisher’s reliance on Jolles, Nelson, and Cross, cases which found utility in certain claimed pharmaceutical compounds, is misplaced. In Jolles, the applicant filed an application claiming naphthacene compounds useful in treating acute myeloblastic leukemia. To support the asserted utility, the applicant presented in vivo data showing eight of the claimed compounds effectively treated tumors in a mouse model. Our predecessor court reversed the Board’s affirmance of the final rejection for lack of utility, finding that the structural similarity between the compounds tested in vivo and the

remaining claimed compounds was sufficient to establish utility for the remaining claimed compounds. Jolles, 628 F.2d at 1327-28.

In Nelson, decided by the Court of Customs and Patent Appeals in the same year as Jolles, Nelson claimed prostaglandin compounds. The PTO declared an interference with an application filed by Bowler claiming the same compounds. The issue before the Board was whether Nelson had established utility for the claimed prostaglandins as smooth muscle stimulants and blood pressure modulators via in vivo and in vitro data, specifically, an in vivo rat blood pressure test and an in vitro gerbil colon smooth muscle stimulation test. The Board declined to award priority to Nelson, characterizing Nelson's tests as "rough screens, uncorrelated with actual utility [in humans]." Our predecessor court reversed, concluding that "tests evidencing pharmacological activity may manifest a practical utility even though they may not establish a specific therapeutic use." Nelson, 626 F.2d at 856.

In Cross, decided by the Federal Circuit five years after Jolles and Nelson, Iizuka filed an application claiming thromboxane synthetase inhibitors, alleged to be useful in treating inflammation, asthma, hypertension, and other ailments. When Cross filed an application claiming the same compounds two months after Iizuka, the PTO declared an interference. The dispositive issue concerned whether Iizuka's Japanese priority application disclosed utility for the claimed inhibitors. The Board concluded that it offered a sufficient disclosure based upon in vitro data showing strong inhibitory action for thromboxane synthetase for structurally-similar compounds in human or bovine platelet microsomes. We affirmed, reasoning:

Opinions of our predecessor court have recognized the fact that pharmacological testing of animals is a screening procedure for testing

new drugs for practical utility. This in vivo testing is but an intermediate link in a screening chain which may eventually lead to the use of the drug as a therapeutic agent in humans. We perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question. Successful in vitro testing will marshal resources and direct the expenditure of effort to further in vivo testing of the most potent compounds, thereby providing an immediate benefit to the public, analogous to the benefit provided by the showing of an in vivo utility.

Cross, 753 F.2d at 1050 (citations omitted).

The facts in these three cases are readily distinguishable from the facts here. In Jolles, Nelson, and Cross, the applicants disclosed specific pharmaceutical uses in humans for the claimed compounds and supported those uses with specific animal test data, in vitro, in vivo, or both. In contrast, Fisher disclosed a variety of asserted uses for the claimed ESTs, but failed to present any evidence – test data, declaration, deposition testimony, or otherwise – to support those uses as presently beneficial and hence practical. Fisher did not show that even one of the claimed ESTs had been tested and successfully aided in identifying a polymorphism in the maize genome or in isolating a single promoter that could give clues about protein expression. Adopting the language of the Cross court, the alleged uses in Jolles, Nelson, and Cross were not “nebulous expressions, such as ‘biological activity’ or ‘biological properties’ [alleged in the application in Kirk],” that “convey little explicit indication regarding the utility of a compound.” Cross, 753 F.2d at 1048. Instead, the alleged uses in those cases gave a firm indication of the precise uses to which the claimed compounds could be put. For example, in Nelson, the claimed prostaglandins could be used to stimulate smooth muscle or modulate blood pressure in humans as shown by both in vivo and in vitro animal data. Hence, the Jolles, Nelson, and Cross courts concluded that the claimed

pharmaceutical compounds satisfied the specific and substantial utility requirements of § 101. We cannot reach that same conclusion here. Fisher's laundry list of uses, like the terms "biological activity" or "biological properties" alleged in Kirk, are nebulous, especially in the absence of any data demonstrating that the claimed ESTs were actually put to the alleged uses.

Fisher's reliance on the commercial success of general EST databases is also misplaced because such general reliance does not relate to the ESTs at issue in this case. Fisher did not present any evidence showing that agricultural companies have purchased or even expressed any interest in the claimed ESTs. And, it is entirely unclear from the record whether such business entities ever will. Accordingly, while commercial success may support the utility of an invention, it does not do so in this case. See Raytheon Co. v. Roper Corp., 724 F.2d 951, 959 (Fed. Cir. 1983) (stating that proof of a utility may be supported when a claimed invention meets with commercial success).

3.

As a final matter, we observe that the government and its amici express concern that allowing EST patents without proof of utility would discourage research, delay scientific discovery, and thwart progress in the "useful Arts" and "Science." See U.S. Const. art. I, § 8, cl. 8. The government and its amici point out that allowing EST claims like Fisher's would give rise to multiple patents, likely owned by several different companies, relating to the same underlying gene and expressed protein. Such a situation, the government and amici predict, would result in an unnecessarily convoluted licensing environment for those interested in researching that gene and/or protein.

The concerns of the government and amici, which may or may not be valid, are not ones that should be considered in deciding whether the application for the claimed ESTs meets the utility requirement of § 101. The same may be said for the resource and managerial problems that the PTO potentially would face if applicants present the PTO with an onslaught of patent applications directed to particular ESTs. Congress did not intend for these practical implications to affect the determination of whether an invention satisfies the requirements set forth in 35 U.S.C. §§ 101, 102, 103, and 112. They are public policy considerations which are more appropriately directed to Congress as the legislative branch of government, rather than this court as a judicial body responsible simply for interpreting and applying statutory law. Under Title 35, an applicant is entitled to a patent if his invention is new, useful, nonobvious, and his application adequately describes the claimed invention, teaches others how to make and use the claimed invention, and discloses the best mode for practicing the claimed invention. What is more, when Congress enacted § 101, it indicated that “anything under the sun that is made by man” constitutes potential subject matter for a patent. S. Rep. No. 82-1979, at 7 (1985). Policy reasons aside, because we conclude that the utility requirement of § 101 is not met, we hold that Fisher is not entitled to a patent for the five claimed ESTs.

B. Enablement

Fisher asserts that we should reverse the enablement rejection upheld by the Board since the Board made it contingent upon the utility rejection, which Fisher argues was not supported by substantial evidence for reasons analyzed above. The government argues to the contrary, asserting that claim 1 of the '643 application cannot

be enabled because the claimed ESTs were not disclosed as having a specific and substantial utility. We agree with the government. It is well established that the enablement requirement of § 112 incorporates the utility requirement of § 101.

The how to use prong of section 112 incorporates as a matter of law the requirement of 35 U.S.C. § 101 that the specification disclose as a matter of fact a practical utility for the invention. If the application fails as a matter of fact to satisfy 35 U.S.C. § 101, then the application also fails as a matter of law to enable one of ordinary skill in the art to use the invention under 35 U.S.C. § 112.

Ziegler, 992 F.2d at 1200-01 (citations omitted); see also Kirk, 376 F.2d at 942 (“Necessarily, compliance with § 112 requires a description of how to use presently useful inventions, otherwise an applicant would anomalously be required to teach how to use a useless invention.”); In re Brana, 51 F.3d 1560, 1564 (Fed. Cir. 1995) (“Obviously, if a claimed invention does not have utility, the specification cannot enable one to use it.”); Manual of Patent Examining Procedure § 2107.01. Here, in light of our conclusion that the Board’s decision with respect to utility applied the correct legal standard and was supported by substantial evidence, we conclude that Fisher failed to satisfy the enablement requirement. Consequently, we leave undisturbed the enablement rejection of the ’643 application under § 112, first paragraph.

III. CONCLUSION

We conclude that substantial evidence supports the Board’s findings that each of the five claimed ESTs lacks a specific and substantial utility and that they are not enabled. Accordingly, the Board’s decision affirming the final rejection of claim 1 of the ’643 patent for lack of utility under § 101 and lack of enablement under § 112, first paragraph, is affirmed.

AFFIRMED

United States Court of Appeals for the Federal Circuit

04-1465
(Serial No. 09/619,643)

IN RE DANE K. FISHER and RAGHUNATH V. LALGUDI

RADER, Circuit Judge, dissenting.

This court today determines that expressed sequence tags (ESTs) do not satisfy 35 U.S.C. § 101 unless there is a known use for the genes from which each EST is transcribed. While I agree that an invention must demonstrate utility to satisfy § 101, these claimed ESTs have such a utility, at least as research tools in isolating and studying other molecules. Therefore, I respectfully dissent.

Several, if not all, of Fisher's asserted utilities claim that ESTs function to study other molecules. In simple terms, ESTs are research tools. Admittedly ESTs have use only in a research setting. However, the value and utility of research tools generally is beyond question, even though limited to a laboratory setting. See U.S. Pat. & Trademark Off., Manual of Patent Examining Procedure (MPEP) § 2107.01 at 2100-33 (8th ed. 2001, rev. Feb. 2003) ("Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility (e.g., they are useful in analyzing compounds)."). Thus, if the claimed ESTs qualify as research tools, then they have a "specific" and "substantial" utility sufficient for § 101. If these ESTs do not enhance research, then Brenner v. Manson, 383 U.S. 519 (1966) (involving the patentability of methods for producing compounds having no known use) controls and erects a § 101 bar for lack of utility. For

the following reasons, these claimed ESTs are more akin to patentable research tools than to the unpatentable methods in Brenner.

In Brenner, the Court confronted a growing conflict between this court's predecessor, the Court of Customs and Patent Appeals (CCPA), and the Patent Office over the patentability of methods of producing compounds with no known use. This conflict began with In re Nelson, 280 F.2d 172 (CCPA 1960), the first in a series of cases wherein the CCPA reversed several Patent Office utility rejections. Brenner, 383 U.S. at 530. Brenner put an end to these cases because, in the 1960s, the Court could not distinguish between denying patents to compounds with no known use and denying patents to methods of producing those useless compounds. The Court commented:

We find absolutely no warrant for the proposition that although Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing, a different set of rules was meant to apply to the process which yielded the unpatentable product. That proposition seems to us little more than an attempt to evade the impact of the rules which concededly govern patentability of the product itself.

Id. at 535. This court's predecessor later extended Brenner to bar patents on compounds as intermediates in the preparation of other compounds having no known use. See In re Kirk, 376 F.2d 936 (CCPA 1967) (rejecting intermediaries for steroids with no known use). These cases, however, share a common underpinning - a method of producing a compound with no known use has no more benefit to society than the useless compound itself.

This case is very different. Unlike the methods and compounds in Brenner and Kirk, Fisher's claimed EST's *are* beneficial to society. As an example, these research tools "may help scientists to isolate the particular underlying protein-encoding genes . . . [with the] overall goal of such experimentation . . . presumably [being] to understand the

maize genome[.]” Majority Opinion, slip op. at 13. They also can serve as a probe introduced into a sample tissue to confirm “that the gene corresponding to the EST was being expressed in the sample tissue at the time of mRNA extraction.” Id., slip op. at 3.

These research tools are similar to a microscope; both take a researcher one step closer to identifying and understanding a previously unknown and invisible structure. Both supply information about a molecular structure. Both advance research and bring scientists closer to unlocking the secrets of the corn genome to provide better food production for the hungry world. If a microscope has § 101 utility, so too do these ESTs.

The Board and this court acknowledge that the ESTs perform a function, that they have a utility, but proceed quickly to a value judgment that the utility would not produce enough valuable information. The Board instead complains that the information these ESTs supply is too “insubstantial” to merit protection. Yet this conclusion denies the very nature of scientific advance. Science always advances in small incremental steps. While acknowledging the patentability of research tools generally (and microscopes as one example thereof), this court concludes with little scientific foundation that these ESTs do not qualify as research tools because they do not “offer an immediate, real world benefit” because further research is required to understand the underlying gene. This court further faults the EST research for lacking any “assurance that anything useful will be discovered in the end.” These criticisms would foreclose much scientific research and many vital research tools. Often scientists embark on research with no assurance of success and knowing that even success will demand “significant additional research.”

Nonetheless, this court, oblivious to the challenges of complex research, discounts these ESTs because it concludes (without scientific evidence) that they do not supply enough information. This court reasons that a research tool has a “specific” and “substantial” utility *only* if the studied object is readily understandable using the claimed tool - that no further research is required. Surely this cannot be the law. Otherwise, only the final step of a lengthy incremental research inquiry gets protection.

Even with a microscope, significant additional research is often required to ascertain the particular function of a “revealed” structure. To illustrate, a cancerous growth, magnified with a patented microscope, can be identified and distinguished from other healthy cells by a properly trained doctor or researcher. But even today, the scientific community still does not fully grasp the reasons that cancerous growths increase in mass and spread throughout the body,¹ or the nature of compounds that interact with them, or the interactions of environmental or genetic conditions that contribute to developing cancer. Significant additional research is required to answer these questions. Even with answers to these questions, the cure for cancer will remain in the distance. Yet the microscope still has “utility” under § 101. Why? Because it takes the researcher one step closer to answering these questions. Each step, even if

¹ ESTs have already been used to advance cancer research well beyond what is achievable using microscopes alone. See Andy J. Minn, Genes That Mediate Breast Cancer Metastasis To Lung, Nature, July 28, 2005 at 518-24 (discussing research to identify genes that mark and mediate breast cancer metastasis to the lung).

small in isolation, is nonetheless a benefit to society sufficient to give a viable research tool “utility” under § 101. In fact, experiments that fail still serve to eliminate some possibilities and provide information to the research process.

The United States Patent Office, above all, should recognize the incremental nature of scientific endeavor. Yet, in the interest of easing its administrative load, the Patent Office will eliminate some research tools as providing “insubstantial” advances. How does the Patent Office know which “insubstantial” research step will contribute to a substantial breakthrough in genomic study? Quite simply, it does not.

In addition, this court faults Fisher for not presenting evidence of utility showing that the claimed ESTs “have been used in the real world.” To the contrary, this court misapprehended the proper procedure. Fisher asserted seven different utilities. The Board rejected two of these assertions outright as “insubstantial.” See Ex parte Fisher, App. No. 2002-2046, slip. op at 14-16 (Bd. Pat. App. and Int. 2004) (acknowledging that the ESTs may be able to detect “the absence of a polymorphism” and “to isolate nucleic acid molecules of other plants and organisms[,]” but finding such utilities are not “substantial” even if the ESTs can perform them). This summary dismissal deprived Fisher of any chance to proffer evidence. Rather than fault Fisher for not presenting evidence it was prevented from offering, this court should instead observe that the Board did not satisfy its burden of challenging Fisher’s presumptively correct assertion that the ESTs were *capable* of performing those functions. See MPEP § 2107.02(IV) at 2100-40 (noting that the initial burden is on the office to establish a prima facie case as to lack of utility and to provide evidentiary support thereof); In re Brana, 51 F.3d 1560, 1566 (Fed. Cir. 1995) (where an applicant has asserted utility in the disclosure, the

Patent Office has the initial burden of challenging this presumptively correct assertion of utility).

Abandoning the proper legal procedure, the Board reasoned that the molecules studied with these ESTs showed no particular use, therefore the ESTs themselves also lacked a utility. In so ruling, the Board did not reject Fisher's utilities on the basis that the ESTs were *unable to perform* the purported utilities. Thus, the Board did not establish a prima facie challenge to the ESTs' ability to perform these two utilities. Without anything to rebut, Fisher had no obligation or opportunity to provide evidence in rebuttal. Thus, I respectfully disagree with this court's conclusion that the Board's decision can be affirmed on the basis that Fisher did not supply evidence of the ESTs' ability to perform the asserted utilities.

In truth, I have some sympathy with the Patent Office's dilemma. The Office needs some tool to reject inventions that may advance the "useful arts" but not sufficiently to warrant the valuable exclusive right of a patent. The Patent Office has seized upon this utility requirement to reject these research tools as contributing "insubstantially" to the advance of the useful arts. The utility requirement is ill suited to that task, however, because it lacks any standard for assessing the state of the prior art and the contributions of the claimed advance. The proper tool for assessing sufficient contribution to the useful arts is the obviousness requirement of 35 U.S.C. § 103. Unfortunately this court has deprived the Patent Office of the obviousness requirement for genomic inventions. See In re Deuel, 51 F.3d 1552 (Fed. Cir. 1995); Martin J. Adelman et al., Patent Law, 517 (West Group 1998) (commenting that scholars have been critical of Deuel, which "overly favored patent applicants in biotech by adopting an

overly lax nonobviousness standard.” (citing Anita Varma & David Abraham, DNA Is Different: Legal Obviousness and the Balance Between Biotech Inventors and the Market, 9 Harv. J. L. & Tech. 53 (1996)); Philippe Ducor, The Federal Circuit and In re Deuel: Does §103 apply to Naturally Occurring DNA?, 77 J. Pat. & Trademark Off. Soc’y 871, 883 (Nov. 1995) (“The Court of Appeals for the Federal Circuit could have formulated its opinion in only one sentence: ‘35 U.S.C. § 103 does not apply to newly retrieved natural DNA sequences.’”); Philippe Ducor, Recombinant Products and Nonobviousness: A Typology, 13 Santa Clara Computer and High Tech. L.J. 1, 44-45 (Feb. 1997) (“This amounts to a practical elimination of the requirement for nonobviousness for these products, even when all the information necessary to discover them is previously available.”); see also over fifty additional articles critical of Deuel in the “Citing References” tab for Deuel on Westlaw. Nonetheless, rather than distort the utility test, the Patent Office should seek ways to apply the correct test, the test used world wide for such assessments (other than in the United States), namely inventive step or obviousness.

Thus, for the foregoing reasons, I would find that Fisher’s asserted utilities qualify the claimed ESTs as research tools useful in the study of other molecules. Because research tools provide a cognizable benefit to society, much like a microscope, the ESTs claimed here have “utility” under § 101. In addition, the enablement rejection should also be reversed because it was a consequence of the finding of lack of utility.

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The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 17

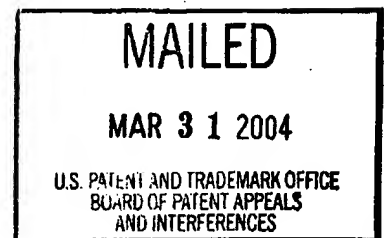
UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte DANE K. FISHER, and RAGHUNATH V. LALGUDI

Appeal No. 2002-2046
Application No. 09/619,643

HEARD: March 16, 2004



Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

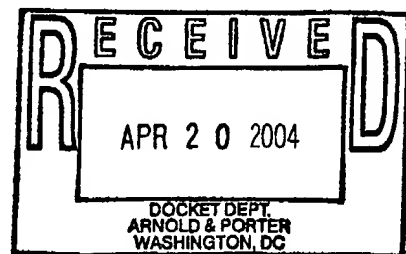
ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claim 1, the only claim pending in the application, reproduced below:

1. A substantially purified nucleic acid molecule that encodes a maize protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO:5.

The examiner does not rely on a reference.



GROUND OF REJECTION

Claim 1 stands rejected under 35 U.S.C. § 101 as lacking utility and § 112, first paragraph, for lack of enablement based on the finding of lack of utility. Claim 1 also stands rejected under 35 U.S.C. § 112, first paragraph, as the specification fails to provide an adequate written description of the claimed invention. We affirm the utility and enablement rejections. We reverse the written description rejection.

BACKGROUND

The subject matter of the present appeal is directed to expressed sequence tags (ESTs). See Specification, page 15, lines 9-10. ESTs "are short sequences of randomly selected clones from a cDNA (or complementary DNA) library which are representative of the cDNA inserts of these randomly selected clones." Specification, page 1.

As set forth at page 9, lines 2-4, of appellants' specification "[t]he present invention provides a substantially purified nucleic acid molecule that encodes a maize protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 32236." Of these 32,236 nucleic acid sequences, the originally filed claims were directed to SEQ ID NO: 1 through SEQ ID NO: 4,013. On January 26, 2001 (Paper No. 4), the examiner entered a Restriction requirement into the record, requiring, inter alia, appellants "to elect up to 5 nucleic acid sequences" for consideration on the merits. Paper No. 4, page 3. In response, appellants elected SEQ ID NO: 1 through SEQ ID NO: 5. The ESTs set forth in SEQ ID NO: 1 through SEQ ID NO:

5 are disclosed to be obtained from cDNA library LIB3115 "generated from maize (RX601, Asgrow Seed Company, Des Moines, Iowa U.S.A.) pooled leaf tissue...." Specification, pages 79-80, Example 1.

The specification sets forth a number of utilities for the nucleic acid molecules of SEQ ID NO: 1 through SEQ ID NO: 5 which are summarized by the examiner (Answer, bridging paragraph, pages 5-6) as follows:

The specification teaches that the nucleic acids may be used to produce a plant containing reduced levels of a protein (pg. 11), determining an association between a polymorphism and a plant trait (pg. 11), isolating a genetic region or nucleic acid (pg. 11), determining a level or pattern in a plant cell of a protein in a plant (pg. 11), determining a mutation in a plant whose presence is predictive of a mutation affecting a level or pattern of a protein (pg. 13), as molecular tags to isolate genetic regions, isolate genes, map genes, and determine gene function (pg. 14), and identifying tissues (pg. 14)[.] The specification states that the nucleic acid ESTs of the present invention can enable the acquisition of molecular markers, which can be used in breeding schemes, genetic and molecular mapping and cloning of agronomically significant genes (pg. 31).

In the examiner's opinion "[t]hese are non-specific uses that are applicable to nucleic acids in general and not particular or specific to the nucleic acids being claimed." Answer, page 6. For example, the examiner finds (Answer, page 10), "determining whether the claimed nucleic acids have or do not have a polymorphism would require determining whether there was a polymorphism within such a sequence and then determining how to use this information in a patentably meaningful way."¹

¹ During the Oral Hearing, appellants' representative confirmed that the administrative file contained no evidence that the claimed ESTs were capable of detecting a polymorphism that correlated with any particular trait.

In presenting their case on appeal, appellants focus on use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism, and their use as probes or as a source for primers. See e.g., Brief, pages 6-12. According to appellants (Brief, page 3), "they have disclosed nucleic acid molecules which, in their current form, provide at least one specific benefit to the public, for example the ability to identify the presence or absence of a polymorphism in a population of maize plants." Furthermore, appellants assert (Brief, page 8), "[t]he specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms...."

CLAIM CONSTRUCTION

As set forth above, claim 1 on appeal is drawn to a substantially purified nucleic acid molecule that encodes a maize protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO:5. According to appellants' specification (page 15, lines 19-25), the term "substantially purified"

refers to a molecule separated from substantially all other molecules normally associated with it in its native state. More preferably a substantially purified molecule is the predominant species present in a preparation. A substantially purified molecule may be greater than 60% free, preferably 75% free, more preferably 90% free, and most preferably 95% free from the other molecules (exclusive of solvent) present in the natural mixture. The term "substantially purified" is not intended to encompass molecules present in their native state.

As we understand the claimed invention the use of the transitional term "comprising" does not allow for internal alterations (e.g. insertions or deletions) of

the nucleotide sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5, but instead only allows for the addition of nucleotides or other molecules at either end of the nucleotide sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5.² In this regard, we recognize, as does the examiner (Answer, page 14), the claim as written encompasses, inter alia, genes, full open reading frames, fusion constructs, and cDNAs.

Accordingly, for the purposes of our review, we interpret the claimed invention as drawn to a nucleic acid molecule, separated from substantially all other molecules normally associated with it in its native state, selected from the group consisting of the nucleic acid molecule defined by the 429 nucleotide sequence set forth in SEQ ID NO: 1, the 413 nucleotide sequence set forth in SEQ ID NO: 2, the 365 nucleotide sequence set forth in SEQ ID NO: 3, the 414 nucleotide sequence set forth in SEQ ID NO: 4, and the 333 nucleotide sequence set forth in SEQ ID NO: 5, with or without any preceding or trailing nucleotides, or other molecules.

DISCUSSION

Utility

The starting point for determining whether a nucleic acid molecule selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 5

² This interpretation of the claimed invention was confirmed by appellants' representative during the Oral Hearing.

possesses utility under 35 U.S.C. § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). As set forth in Brenner, at 534-35, 148 USPQ at 695³,

the basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until [an invention] is refined and developed to this point--where specific benefit exists in currently available form--there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

In considering the issues presented in this appeal, special attention must be paid to the Brenner court's statement that a patent should issue only when an invention possesses "substantial utility," i.e., "where a specific benefit exists in currently available form." Whether a claimed invention is useful under 35 U.S.C. § 101 is a question of fact. Cross v. Iizuka, 753 F.2d 1040, 1044 n.7, 224 USPQ 739, 742 n.7 (Fed. Cir. 1985).

At issue in Brenner was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that "where a claimed process produces a

³ In discussing the issue of utility under 35 U.S.C. § 101, the Federal Circuit and the Court of Customs and Patent Appeals since Brenner, have used the phrases "substantial utility" and "practical utility" interchangeably. See e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1963-1964, 39 USPQ2d 1895, 1898-1899 (Fed. Cir. 1996) ("It is well established that a patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed.").

known product it is not necessary to show utility for the product.” Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be “useful,” that “simple, everyday word can be pregnant with ambiguity when applied to the facts of life.” Id. at 529, 148 USPQ at 693. Thus,

[i]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the “new and useful” phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man’s grasp and where little or nothing is wholly beyond the pale of “utility”—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.⁴

The Court, finding “no specific assistance in the legislative materials underlying § 101,” based its analysis on “the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other.” Id. at 532, 148 USPQ at 695. The Court concluded that “[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.” Id. at 534-35, 148 USPQ at 695.

⁴ The invention at issue in Brenner was a process, but the Court expressly noted that its holding “would apply equally to the patenting of the product produced by the process.” Id. at 535, 148 USPQ at 695-96.

The Court considered and rejected the applicant's argument that attenuating the requirement of utility "would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge." The Court noted that, while there is value to encouraging disclosure, "a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of

§ 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroidal research and in the application of steroidal materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the

researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" Id. at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. Id. "[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there." Id.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in

cancer chemotherapy.” Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were “relevant to the treatment of humans and [were] not to be disregarded,” id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that “[it] is axiomatic that an invention cannot be considered ‘useful,’ in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious.” Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court “perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question.” Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by “marshal[ing] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds ..., analogous to the benefit provided by the showing of an in vivo utility.” Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar

compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best ... on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, at 1203, 26 USPQ2d at 1605.

With these principles in mind we turn to the issues at hand. Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal, i.e., identification and detection of polymorphisms and use

as probes or as a source for primers. We shall focus on these asserted utilities first and then address the other arguments set forth in the briefing.

a. Polymorphisms

This utility is discussed at pages 35-42 of the specification in terms of what polymorphisms are and how one would go about determining the existence of a polymorphism. The discussion in this portion of the specification, however, is not specific to the nucleotide molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5. To the contrary, according to appellants' specification (page 35, lines 25-26), "one or more of the [32,236] EST nucleic acid molecules (or a sub-fragment thereof) may be employed as a marker nucleic acid molecule to identify ... polymorphism(s)." The specification does not explain why any of the 32,236 nucleotide molecules disclosed in the specification, or more specifically the five nucleotide molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5, would in fact be useful in detecting polymorphisms.

Rather, appellants argue (Brief, page 7), "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." In other words, appellants' position is that an EST by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by an EST, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage. As the examiner explains (Answer, bridging paragraph, pages 10-11):

Polymorphisms are natural variations within sequences which themselves may not have any meaningful use. Therefore, determining whether the claimed nucleic acids [(or nucleic acids detected by the claimed nucleic acids)] have or do not have a polymorphism would require determining whether there was a polymorphism within such a sequence and then determining how to use this information in a patentably meaningful way. The [a]ppellant also argues, "many of these uses are directly analogous to a microscope". This argument has been reviewed but is not convincing because the microscope provides information to the scientist which is automatically useful. For example, the microscope may be used for identification and differentiation between gram-positive and gram-negative bacteria. The differentiation of bacteria facilitates in the administration of proper antibiotics. For example, if the microscope is used to determine whether Staph is present or whether Strep is present provides valuable information to the scientist and/or doctor for treating patients. The instant invention, however, provides no information to this extent. If the scientist determines that SEQ ID NO: 1 is present, the scientist does not know how to use this information. Thus, the identification of SEQ ID NO: 1 is not a substantial utility.

In contrast, at the other end of the "utility spectrum" would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene from which the EST is derived has in the development and/or phenotype of the plant. Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the gene and its role in the plant's development and/or phenotype lies the line between "utility" and "substantial utility." We need not draw the line or further

define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.

b. Probes or source of primers

Appellants argue that the "specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms...." Appeal Brief, page 8. While that may be true, it begs the question of what substantial use such nucleic acid molecules would have? Again, the present specification does not attribute any property in terms of plant trait, or phenotype to any of the nucleotide molecules set forth in SEQ ID NO: 1 through SEQ ID NO: 5. In the absence of such information, using the claimed molecules to isolate other molecules, which themselves lack substantial utility, does not represent a substantial utility.

Appellants also assert that the claimed nucleic acid molecules may be used in a "chromosome walk." Brief, pages 8-9. According to appellants (Brief, page 9),

The claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter that is active in leaves at the time of anthesis. Isolation of such a promoter would be desirable and particularly useful because it allows expression of proteins at that important developmental state, including proteins that provide disease resistance. Because the claimed nucleic acid molecules were isolated from leaves, they provide an appropriate starting point for isolating a promoter active in leaves. A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter.

As we understand this argument, the claimed ESTs may be useful in searching for promoters that are only active in leaves at the time of anthesis. The

specification, however, fails to demonstrate that any of the nucleic acid molecules set forth in SEQ ID NO: 1 through SEQ ID NO: 5 would be useful in obtaining a successful result from such a search. As set forth at page 34, lines 14-19 of appellants' specification,

The [32,236] nucleic acid molecules of the present invention may be used to isolate promoters of tissue enhanced[,] tissue specific, cell-specific, cell -type, developmentally or environmentally regulated expression profiles. Isolation and functional analysis of the 5' flanking promoter sequences of these genes from genomic libraries, for example, using genomic screening methods and PCR techniques would result in the isolation of useful promoters and transcriptional regulatory elements.

The specification does not provide any expectation of successfully using any of the 32,236 nucleic acid molecules disclosed in the specification, or more specifically the five nucleic acid molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5, to isolate promoters of tissue enhanced, tissue specific, cell-specific, cell-type, developmentally or environmentally regulated expression profiles.

Furthermore, notwithstanding appellants' assertion (Brief, page 9), there is no evidence on this record that any of the nucleic acid molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5 are tissue or cell-type specific, or developmentally or environmentally regulated. In this regard, we note that the claimed nucleic acid molecules were isolated from the cDNA library LIB3115. Specification, page 80, lines 5-6. There is no evidence on this record that LIB3115 is a subtractive cDNA library, wherein nucleic acid molecules from other maize tissue, or from other developmental stages, was subtracted (removed)

from the library. Compare, for example, the subtractive cDNA library LIB3153 which is disclosed (specification, page 83, lines 17-19) to be "generated by subtracting driver cDNA, which is prepared from kernels harvested from 15 DAP [days after pollination] maize plants, from target cDNA, which is prepared from endosperms harvested from 5-8 day[s] after pollination (DAP) maize plants." In contrast to the claimed nucleic acid molecules, nucleic acid molecules SEQ ID NO: 24,931 through SEQ ID NO: 25,680 are from the subtractive cDNA library LIB3153.

In our opinion, the claimed nucleic acid molecules having the sequences identified as SEQ ID NO: 1 through SEQ ID NO: 5, represent five randomly selected nucleic acid molecules isolated from pooled leaf tissue at the time of anthesis. Notwithstanding appellants' emphasis on "anthesis," for the foregoing reasons, we find no evidence on this record that any of appellants' five randomly selected nucleic acid molecules are expressed only at the time of "anthesis." Accordingly, despite appellants' assertion to the contrary, there is no reasonable expectation that any of the claimed nucleic acid molecules would be capable of isolating a promoter that was only active in leaves at the time of anthesis. As appellants recognize (Brief, page 9), "[a] random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter" compared to a nucleic acid molecule that is known to be specifically associated with this stage of plant development.

We recognize appellants' argument (Brief, bridging sentence, pages 9-10), "[a]n invention may be 'less effective than existing devices but nevertheless

meet the statutory criteria for patentability.' Custom Accessories, Inc. v. Jeffrey-Allan Indus., 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986)." While we agree with appellants' statement, we fail to see how it applies to appellants' claimed invention, wherein there is no evidence or expectation that the claimed nucleic acid molecules would be "effective" at all. In this regard, we remind appellants that an invention does not have utility sufficient to satisfy § 101 until it is "refined and developed" to the point of providing a specific benefit in currently available form. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695.

An invention certainly can have a utility that is shared by other compounds or compositions. Take, for example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful as analgesics. On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

c. Other Arguments

Appellants argue that the specification "discloses additional utilities for the claimed nucleic acid molecules including introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for compounds such as a herbicide." Brief, page 6. Specifically, appellants argue (id.) that "a compound can be provided to both an antisense plant and a control plant (no antisense) and the effect of the compound on the plant can be monitored." Appellants analogize this proposed procedure to a "cell-based assay" which appellants assert to have a "legally sufficient utility." Id.

Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. The portion of the specification cited in support of this argument (page 73, line 17 through page 74, line 17) indicates that the nucleic acid molecule must be introduced into a plant cell and transcribed using an appropriate promoter to result in the suppression of an endogenous protein. The specification does not indicate that such a method is feasible when the nucleic acid to be used is uncharacterized⁵ as here. Such a use does not provide a specific or substantial benefit in currently available form.

Appellants also argue that the claimed nucleic acids are useful to measure the level of mRNA in a sample through use of microarray technology

⁵ To emphasize the uncharacterized nature of appellants' invention we note the examiner's finding (Answer, page 17) that translating SEQ ID NO: 5 in all 6 possible reading frames reveals that the sequence contains numerous stop codons which would terminate the translation of a protein, or protein fragment, encoded thereby.

and use as molecular markers. Brief, page 6. In regard to microarrays, appellants argue (id. fn. 3) that it is "standard practice" to screen populations of nucleic acids with EST sequences without characterizing each and every target mRNA. We find that the asserted utility of the claimed nucleic acid—as one component of an assay for monitoring gene expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form. We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid depicted in e.g., SEQ ID NO: 1. However, the specification provides no guidance that would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification simply provides no guidance regarding what the SEQ ID NO: 1-specific information derived from a gene expression experiment would mean. As the examiner points out (Answer, page 9), "the instant claimed nucleic acids appear to require further experimentation on the material itself to determine the function and properties of the claimed nucleic acids."

To highlight the examiner's assertion, suppose, for example, that a researcher found that SEQ ID NO: 1 expression was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. Maybe the meaning in a change in SEQ ID NO: 1 expression would depend on other factors, but again the specification provides no hint as to what other factors

might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), the degree of increase? The specification simply provides no guidance as to how to interpret the results that might be seen using SEQ ID NO: 1 in a gene expression assay.

In effect, appellants' position is that the claimed nucleic acids are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the present case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, because even if used in gene expression assays, the specification does not disclose how to use SEQ ID NO: 1-specific gene expression data.

Assuming arguendo, that a generic gene expression assay—one based on monitoring expression of thousands of uncharacterized nucleic acids would provide a useful tool for, e.g., drug discovery, it does not follow that each one of

the nucleic acids represented in the assay individually has patentable utility.

Although each nucleic acid in the assay contributes to the data generated by the assay overall, the contribution of a single nucleic acid—its data point—is only a tiny contribution to the overall picture. The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently available form.

Providing a single data point among thousands or millions, even if the thousands or millions of data points collectively are useful, does not meet this standard.

The Supreme Court noted that the patent system contemplates a basic quid pro quo: in exchange for the legal right to exclude others from his invention for a period of time, an inventor discloses his invention to the public. See Brenner, 383 U.S. at 534, 148 USPQ at 695. The Brenner Court held that the grant of patent rights to an applicant is justified only by disclosure of an invention with substantial utility – a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the applicant has not met his side of the bargain, and has not provided a disclosure sufficient to justify a grant of the right to exclude others. See id.

We reach the same conclusion in regard to appellants' assertion that the nucleic acid molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5 are

useful as a molecular marker or probe. It is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of SEQ ID NO: 1 as a molecular marker or probe represents a substantial use.

Appellants argue that ESTs have real world value as seen from the "growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs." Brief, page 11. Since appellants fail to provide any suggestion on which use of ESTs this industry is premised on, we can only assume that appellants are referring to the potential usefulness of EST databases, clone sets or microarrays. Suffice it to say, the claims on appeal are not directed to EST databases, clone sets and/or microarrays. Again, it is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecules of SEQ ID NO: 1 through SEQ ID NO: 5 in such devices represents a substantial use.

For the foregoing reasons we affirm the rejection of claim 1 under 35 U.S.C. § 101.

Enablement

According to the examiner (Answer, page 13, emphasis removed), "since the claimed invention is not supported by either a specific, substantial asserted utility or a well established utility for the reasons set forth [in support of the rejection under 35 U.S.C. § 101] one skilled in the art clearly would not know how to use the claimed invention." This rejection is simply a corollary of the finding of lack of utility. Appellants assert (Brief, page 12), this rejection should be reversed for the same reasons set forth in their arguments regarding the

rejection under 35 U.S.C. § 101. Thus, our conclusion with respect to the § 101 issue will also apply to this aspect of the § 112 (enablement) issue. On this basis we affirm the rejection of claim 1 under the enablement provision of 35 U.S.C. § 112, first paragraph.

Written description

This rejection stands on a different footing. As we understand the examiner's argument the use of the transitional phrase "comprising" in appellants' claimed invention results in appellants claiming a large genus of nucleic acid molecules which are not adequately described by SEQ ID NO: 1 through SEQ ID NO: 5. Answer, pages 13-16. Apparently the examiner is of the opinion that the claimed invention should be limited to nucleic acid molecules as set forth in SEQ ID NO: 1 through SEQ ID NO: 5. In response appellants argue (Brief, page 14, original footnote omitted),

Applicants have provided the nucleotide sequences required by the claims, i.e., SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, and SEQ ID NO: 5, and have thus established possession of the claimed invention. The fact that the claims at issue are intended to cover molecules that include the recited sequences joined with additional sequences⁶ does not mean that [a]pplicants were any less in possession of the claimed nucleic acid molecules.

As discussed supra, as we understand the claimed invention, the use of the transitional term "comprising" does not allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequences set forth in SEQ ID NO: 1

⁶ By way of examples appellants explain (Brief, bridging paragraph, pages 14-15) that the specification discloses, inter alia, the claimed nucleic acid molecules joined together with vectors, and other nucleic acids (e.g. fusion nucleic acid molecules) and detectable labels.

through SEQ ID NO: 5, but instead only allows for the addition of nucleotides or other molecules at either end of the nucleotide sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5. We agree with appellants that they have provided an adequate written description of nucleic acid molecules with the sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5. That the claimed nucleic acid molecules may have other molecules attached to either, or both of their 5' or 3' ends does not diminish appellants' adequate written description of the nucleic acids molecules with the sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5 as claimed.

Accordingly, we reverse the rejection of claim 1 under the written description provision of 35 U.S.C. § 112, first paragraph.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED


William F. Smith

Administrative Patent Judge



Donald E. Adams
Administrative Patent Judge


Eric Grimes

Administrative Patent Judge

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The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 26

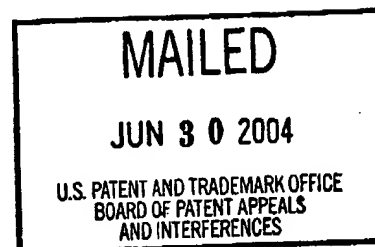
UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte DAVID K. KOVALIC and JINGDONG LIU

Appeal No. 2003-1744
Application No. 09/654,617

HEARD: June 8, 2004



Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

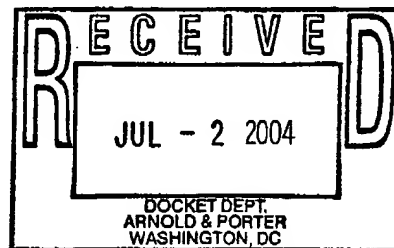
ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 11-17. Claim 12 is illustrative of the subject matter on appeal and is reproduced below:

12. A substantially purified nucleic acid molecule comprising from about 50 to about 100 nucleotide residues of the nucleic acid sequence set forth in SEQ ID NO: 13,782.

The examiner does not rely on a reference.



GROUND OF REJECTION

Claims 11-17 stand rejected under 35 U.S.C. § 101 as lacking utility and § 112, first paragraph, for lack of enablement based on the finding of lack of utility. Claims 11-15 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification fails to provide an adequate written description of the claimed invention. We affirm the utility rejections under 35 U.S.C. § 101 and § 112, first paragraph. Having disposed of all claims on appeal, we do not reach the written description rejection.

BACKGROUND

According to appellants' specification (page 1), "[t]he invention relates to nucleic acid sequences from plant cells, in particular, nucleic acid sequences from maize, teosinte, soybean, Arabidopsis, cotton, sorghum, rice and wheat." The specification also discloses (id., page 13), "[n]ucleic acid molecules of the present invention also include non-maize, non-sorghum, non-cotton and non-teosinte homologues. Preferred plant sources of homologues are selected from the group consisting of alfalfa, barley, Brassica, broccoli, cabbage, citrus, garlic, oat, oilseed rape, onion, canola, flax, an ornamental plant, pea, peanut, pepper, potato, rice, rye, strawberry, sugarcane, sugarbeet, tomato, poplar, pine, fir, eucalyptus, apple, lettuce, lentils, grape, banana, tea, turf grasses, sunflower, oil palm and Phaseolus." More particularly, appellants disclose "[t]he present invention provides a substantially purified nucleic acid molecule where the nucleic acid molecule comprises a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 463,173 or complements

thereof or fragments of either;" or nucleic acid molecules that share between 90% to 100% sequence identity with one or more of the nucleic acid sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 463,173 or complements thereof or fragments of either. See e.g., specification, pages 3 and 11.

The original claims filed with the application were directed to all 463,173 nucleic acid sequences. On August 23, 2001 (Paper No. 6), the examiner entered a Restriction requirement into the record, requiring, inter alia, appellants to elect a single nucleic acid sequence for consideration on the merits. Paper No. 6, page 3. In response, appellants elected SEQ ID NO: 13,782.

CLAIM GROUPING

According to appellants (Brief, page 2), "[p]atentability of claims 11-17 is addressed together in sections 8.A through 8.D below." We understand appellants' statement to mean that claims 11-17 stand or fall together. Accordingly, we limit our discussion to representative independent claim 12. Claims 11 and 13-17 will stand or fall together with claim 12. In re Young, 927 F.2d 588, 590, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991).

CLAIM CONSTRUCTION

As set forth above, claim 12 on appeal is drawn to a substantially purified nucleic acid molecule comprising from about 50 to about 100 nucleotide residues of the nucleic acid sequence set forth in SEQ ID NO: 13,782. According to

appellants' specification (bridging paragraph, pages 8-9), the term "substantially purified"

refers to a molecule separated from substantially all other molecules normally associated with it in its native state. More preferably a substantially purified molecule is the predominant species present in a preparation. A substantially purified molecule may be greater than 60% free, preferably 75% free, more preferably 90% free, and most preferably 95% free from the other molecules (exclusive of solvent) present in the natural mixture. The term "substantially purified" is not intended to encompass molecules present in their native state.

As we understand the subject matter of claim 12 the transitional term "comprising" does not allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequence set forth in SEQ ID NO: 13,782, but instead only allows for the addition of nucleotides or other molecules¹ at either end of the nucleotide sequence set forth in SEQ ID NO: 13,782. In this regard, we recognize, as does the examiner (Answer, page 4), the claim as written encompasses, inter alia, any full length gene, fusion construct, RNA or cDNA that contains about 50 nucleotide to about 100 nucleotide residues of the nucleic acid sequence set forth in SEQ ID NO: 13,782.

Accordingly, for the purposes of our review, we interpret the claimed invention as drawn to a nucleic acid molecule, separated from substantially all other molecules normally associated with it in its native state, that comprises about 50 to about 100 nucleotide residues of the nucleic acid molecule defined

¹ According to appellants' specification (page 9), "agents of the present invention may be labeled with reagents that facilitate detection of the agent (e.g., fluorescent labels, ... chemical labels, ... [and] modified bases...."

by the nucleotide sequence set forth in SEQ ID NO: 13,782 with or without any preceding or trailing nucleotides, or other molecules.

DISCUSSION

Utility

The starting point for determining whether the nucleic acid molecule of claim 12 possesses utility under 35 U.S.C. § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). As set forth in Brenner, at 534-35, 148 USPQ at 695²,

the basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until [an invention] is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

In considering the issues presented in this appeal, special attention must be paid to the Brenner court's statement that a patent should issue only when an invention possesses "substantial utility," i.e., "where a specific benefit exists in currently available form." Whether a claimed invention is useful under 35 U.S.C. § 101 is a question of fact. Cross v. Iizuka, 753 F.2d 1040, 1044 n.7, 224 USPQ 739, 742 n.7 (Fed. Cir. 1985).

² In discussing the issue of utility under 35 U.S.C. § 101, the Federal Circuit and the Court of Customs and Patent Appeals since Brenner, have used the phrases "substantial utility" and "practical utility" interchangeably. See e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1563-1564, 39 USPQ2d 1895, 1898-1899 (Fed. Cir. 1996) ("It is well established that a patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed.").

At issue in Brenner was a claim to “a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced.” Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that “where a claimed process produces a known product it is not necessary to show utility for the product.” Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be “useful,” that “simple, everyday word can be pregnant with ambiguity when applied to the facts of life.” Id. at 529, 148 USPQ at 693. Thus,

[i]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the “new and useful” phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man’s grasp and where little or nothing is wholly beyond the pale of “utility”—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.³

The Court, finding “no specific assistance in the legislative materials underlying § 101,” based its analysis on “the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the

³ The invention at issue in Brenner was a process, but the Court expressly noted that its holding “would apply equally to the patenting of the product produced by the process.” Id. at 535, 148 USPQ at 695-96.

other.” Id. at 532, 148 USPQ at 695. The Court concluded that “[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.” Id. at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant’s argument that attenuating the requirement of utility “would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge.” The Court noted that, while there is value to encouraging disclosure, “a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development.” Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not “mean to disparage the importance of contributions to the fund of scientific information short of the invention of something ‘useful,’” and that it was not “blind to the prospect that

what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroidal research and in the application of steroidal materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" Id. at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. Id. "[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there." Id.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in cancer chemotherapy." Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were "relevant to the treatment of humans and [were] not to be disregarded," id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that "[it] is axiomatic that an invention cannot be considered 'useful,' in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious." Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court "perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for

the compound in question.” Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by “marshal[ing] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds ..., analogous to the benefit provided by the showing of an in vivo utility.” Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101’s requirement that an invention be “useful” is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every “use”

that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best ... on the way to discovering a

practical utility for polypropylene at the time of the filing," but not yet there.

Ziegler, at 1203, 26 USPQ2d at 1605.

On this record, appellants' specification sets forth a number of utilities for the nucleic acid molecules of SEQ ID NO: 1 through SEQ ID NO: 463,173 including their use (1) as markers capable of detecting the level, pattern, occurrence or absence of a biological process, wherein the biochemical process is selected from among 55 different biochemical processes (specification, pages 3 and 16-19); (2) to express proteins from which antibodies can be made to immunoassay for the expressed protein or mimetics thereof (id. at pages 19-23); (3) in transforming or transfecting plants to either overexpress the encoded protein or block the expression of a target gene (id., pages 23-37, particularly page 34, last paragraph and page 35, third full paragraph); (4) to obtain other nucleic acid molecules from the same species, "including nucleic acid molecules that encode the complete coding sequence of a protein and promoters and flanking sequences of such molecules" (id., bridging paragraph, pages 37-38 and page 39); (5) to obtain nucleic acid homologues from other plants or organisms (id., pages 38-39); (6) to detect genetic polymorphisms (id., pages 39-44); (7) to monitor gene expression, e.g. through the use of a microarray (id., pages 44-51); (8) "to determine an attribute or feature (e.g. the presence or absence, location, correlation, etc.) of a molecule, cell, tissue or plant" (id., page 46-47); (9) "to identify a protein or fragment thereof that specifically binds to a nucleic acid molecule of the invention" (id., page 52).

We note, however, that the specification does not specifically disclose how to use a nucleic acid comprising from about 50 to about 100 nucleotide residues of the nucleic acid sequence set forth in SEQ ID NO: 13,782, as set forth in claim 12.⁴ To the contrary, the specification describes the aforementioned utilities as applicable to all of the nucleic acid molecules set forth in SEQ ID NO: 1 through SEQ ID NO: 463,173.

Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal, i.e., identification and detection of polymorphisms and use as probes or as a source for primers. We shall focus on these asserted utilities first and then address the other arguments set forth in the briefing.

a. Polymorphisms

This utility is discussed at pages 40-44 of the specification in terms of what polymorphisms are and how one would go about determining the existence of a polymorphism. The discussion in this portion of the specification, however, is not specific to the nucleotide molecule set forth in claim 12. To the contrary, according to appellants' specification (page 44, lines 7-8), "one or more [of the 463,173] nucleic acid molecule[s] or fragment[s] thereof of the invention can be used as a probe in accordance with the above-described polymorphic methods." The specification does not explain why any of the 463,173 nucleic acid molecules disclosed in the specification, or more specifically a nucleic acid

⁴ On this record, the examiner finds "[t]here is no specific use particularly linked to the nucleic acids of the elected SEQ ID NO." Answer, page 3.

molecule comprising from about 50 to about 100 nucleotide residues of the nucleic acid sequence set forth in SEQ ID NO: 13,782 would in fact be useful in detecting polymorphisms.

Rather, appellants argue (Brief, page 7), "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." In other words, appellants' position is that a nucleic acid by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by a nucleic acid, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage. As the examiner explains (Answer, page 11), appellants' specification defines "polymorphism" as

"a variation or difference in the sequence of the gene or its flanking regions that arises in some members of a species." It follows from this definition that if there is no "variation or difference in the sequence of the gene or its flanking regions" among "members of a species," then no polymorphism exists, i.e. a polymorphism is absent, in this region of the genome.

According to the examiner (Answer, page 10), "the presence or absence of the claimed nucleotide sequence in a sample (or polymorphisms thereof) has no meaning absent some association. Further experimentation is required to

determine what, if any, that meaning or association might be." In this regard, the examiner finds (Answer, page 11), appellants' specification "does not disclose whether the claimed nucleic acid molecules can, in fact, be used to detect any polymorphism whatsoever. Thus, the specification leaves open the possibility that there may be no polymorphism to detect." According to the examiner (Answer, bridging paragraph, pages 11-12), "[t]he specification generally teaches using a polymorphism, detectable with the claimed nucleic acid molecules, as a molecular marker for a linked trait of interest, but fails to teach either the polymorphism or the trait of interest." According to the examiner (Answer, page 13), "the specification fails to identify even one specific polymorphism that can be detected with the claimed nucleic acid molecule, the specification fails to show any specific correspondence between the disclosed general utility and the claimed subject matter, regardless of any specific application requiring detection of polymorphisms." Accordingly the examiner finds (id.), "using the claimed invention to first determine whether or not the claimed nucleic acid molecule can, in fact, detect a polymorphism is to determine whether or not the claimed invention has a utility that requires detecting a polymorphism, i.e. it is 'use testing' and not substantial."

In contrast, at the other end of the "utility spectrum" would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene from which the nucleic acid is derived has in the development and/or phenotype of the plant. Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the

gene and its role in the plant's development and/or phenotype lies the line between "utility" and "substantial utility." We need not draw the line or further define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.⁵

b. Probes or source of primers

Appellants assert that the "specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms...." Brief, page 8. While that may be true, it begs the question of what substantial use such nucleic acid molecules would have? Again, the present specification does not attribute any property in terms of plant trait, or phenotype to the nucleic acid set forth in claim 12. In the absence of such information, using the claimed molecule to isolate other molecules, which themselves lack substantial utility, does not represent a substantial utility.⁶

Appellants also assert that the claimed nucleic acid molecule may be used in a "chromosome walk." Brief, page 8. According to appellants (Brief, page 9),

The claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter that is active in Arabidopsis. A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter. Furthermore, even if a random nucleic acid molecule provided a better starting point than the claimed

⁵ For the foregoing reasons, we disagree with appellants' assertion (Brief, page 3), claimed nucleic acid molecule provides "at least one specific benefit to the public, for example the ability to identify the presence or absence of a polymorphism in a population of Arabidopsis."

⁶ According to the examiner (Answer, page 14), "since further research is needed to determine what, if any, real world utility the 'other nucleic acid molecules' may have, the use of the claimed nucleic acid for obtaining the 'other nucleic acid molecules' falls short of a substantial utility."

nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules.

As we understand this argument, the claimed nucleic acid may be useful in searching for promoters that active in Arabidopsis. The specification, however, fails to demonstrate that the nucleic acid molecule set forth in claim 12 would be useful in obtaining a successful result from such a search. As set forth at page 39, lines 15-20 of appellants' specification,

The [463,173] nucleic acid molecules of the present invention may be used to isolate promoters of cell enhanced, cell specific, tissue enhanced, tissue specific, developmentally or environmentally regulated expression profiles. Isolation and functional analysis of the 5' flanking promoter sequences of these genes from genomic libraries, for example, using genomic screening methods and PCR techniques would result in the isolation of useful promoters and transcriptional regulatory elements.

The specification does not provide any expectation of successfully using any of the 463,173 nucleic acid molecules disclosed in the specification, or more specifically the nucleic acid molecule of claim 12 to isolate promoters of cell enhanced, cell specific, tissue enhanced, tissue specific, developmentally or environmentally regulated expression profiles.

According to the examiner (Answer, page 15), "the specification fails to disclose any characteristics of the corresponding promoter, or any other promoter within 'chromosome walking' distance; neither structural characteristics, by which the promoter might be identified, nor functional characteristics, by which a specific and substantial use for the promoter might be determined." By

way of example, the examiner argues (Answer, page 16), assume

a nucleotide sequence is identified during the chromosome walk as a putative promoter by sequence analysis, is then subcloned into operable linkage with a reporter gene and transfected into an appropriate cells, but found not to express the reporter gene in the cells. This result could mean the putative promoter: is not truly a promoter, i.e. a false positive; is not the corresponding promoter; or is incomplete, i.e. lacked additional sequence elements required for promoter activity in the seed pod cells.

According to the examiner (Answer, page 9), appellants merely isolated the claimed nucleic acid molecule, "[t]hey have not tested, evaluated, or calibrated the claimed nucleotide sequence for any particular use."

We recognize appellants' argument (Brief, page 9), "[a]n invention may be 'less effective than existing devices but nevertheless meet the statutory criteria for patentability.' Custom Accessories, Inc. v. Jeffrey-Allan Indus., 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986)." While we agree with appellants' statement, we fail to see how it applies to appellants' claimed invention, wherein there is no evidence or expectation that the claimed nucleic acid molecules would be "effective" at all. In this regard, we remind appellants that an invention does not have utility sufficient to satisfy § 101 until it is "refined and developed" to the point of providing a specific benefit in currently available form. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695.

An invention certainly can have a utility that is shared by other compounds or compositions. Take, for example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful

as analgesics. On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

c. Other Arguments

Appellants argue that the specification "discloses additional utilities for the claimed nucleic acid molecules including introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for compounds such as a herbicide or traits such as disease resistance." Brief, page 5. Specifically, appellants argue (*id.*) that "a compound can be provided to both an antisense plant and a control plant (no antisense) and the effect of the compound on the plant can be monitored." Appellants analogize this proposed procedure to a "cell-based assay" which appellants assert to have a "legally sufficient utility." Brief, bridging sentence, pages 5-6.

However, the examiner finds (Answer, page 6), further research is required to use of the claimed nucleic acid molecule's use to detect the presence and/or identity of polymorphisms, as hybridization probes for expression profiling,

as antisense inhibitors by introduction of the claimed nucleic acid molecule into a plant or plant cell where the resulting cell or plant is to be used to screen compounds such as herbicides, to measure the level of mRNA in a sample, and as a molecular marker. In addition, the examiner finds (id.), that since targets are not disclosed in the specification, the use of the claimed nucleic acid molecule "as antisense inhibitors would require further experimentation to determine the target of inhibition." To the extent that appellants would argue that the claimed nucleic acid could be used in assays that measure the presence of a material that correlates to a predisposed disease condition, the examiner finds (Answer, page 7), "[t]he instant specification sets forth no such correlation for any condition."

As to the use of the claimed nucleic acid in microarrays (see e.g., Brief, page 6, n. 3), the examiner finds (Answer, page 7), "[a]ppellant is [sic] not claiming microarrays or collections of nucleotides and the specification does not associate the claimed sequence with any trait of interest." According to the examiner (Answer, page 8),

locating and measuring nucleic acid molecules within a sample is not a substantial use because it takes further research to determine any substantial use of the results of locating and measuring. The specification discloses no substantial uses of locating and measuring any nucleic acid molecule that does not consist or comprise SEQ ID NO: 13[,]782.

In addition, the examiner acknowledges appellants' assertion (Brief, page 5, n. 1), "[i]t is irrelevant whether the corresponding mRNA or polypeptide have utility because [a]pplicants are not relying on utility of the mRNA or polypeptide to

establish utility of the claimed nucleic acid molecules." Answer, page 6.

Nevertheless, the examiner asserts (id.), "[t]he [B]rief does not dispute that no open reading frame (ORF), no encoded protein, nor any biological activity for any encoded protein has been disclosed for SEQ ID NO: 13[,1782."

As for non-asserted utilities, the examiner finds (Answer, bridging paragraph, pages 3-4), "[n]either the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid and/or protein compound(s) such that another non-asserted utility would be well established for the elected nucleic acid compound."

Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. In regard to microarrays, we find that the asserted utility of the claimed nucleic acid—as one component of an assay for monitoring gene expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form. We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid molecule set forth in claim 12. However, the specification provides no guidance that would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification simply provides no guidance regarding what the specific information derived from a gene expression experiment would mean in the context of a nucleic acid molecule as set forth in claim 12.

To highlight the examiner's assertion (Answer, pages 7-8), suppose, for example, that a researcher found that expression of the nucleic acid molecule set forth in claim 12 was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. Maybe the meaning in a change in expression would depend on other factors, but again the specification provides no hint as to what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), the degree of increase? The specification simply provides no guidance as to how to interpret the results that might be seen using the nucleic acid molecule of claim 12 in a gene expression assay.

In effect, appellants' position is that the claimed nucleic acids are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the present case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility

because the specification did not disclose how to use the end-product, the products claimed here lack utility, because even if used in gene expression assays, the specification does not disclose how to use the specific gene expression data in the context of the nucleic acid molecule of claim 12.

Assuming arguendo, that a generic gene expression assay - one based on monitoring expression of thousands of uncharacterized nucleic acids - would provide a useful tool for, e.g., drug discovery, it does not follow that each one of the nucleic acids represented in the assay individually has patentable utility. Although each nucleic acid in the assay contributes to the data generated by the assay overall, the contribution of a single nucleic acid—its data point—is only a tiny contribution to the overall picture. The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently available form. Providing a single data point among thousands or millions, even if the thousands or millions of data points collectively are useful, does not meet this standard. The Supreme Court noted that the patent system contemplates a basic quid pro quo: in exchange for the legal right to exclude others from his invention for a period of time, an inventor discloses his invention to the public. See Brenner, 383 U.S. at 534, 148 USPQ at 695. The Brenner Court held that the grant of

patent rights to an applicant is justified only by disclosure of an invention with substantial utility – a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the applicant has not met his side of the bargain, and has not provided a disclosure sufficient to justify a grant of the right to exclude others. See id.

We reach the same conclusion in regard to appellants' assertion that the nucleic acid molecule set forth in claim 12 is useful as a molecular marker or probe. It is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of claim 12 as a molecular marker or probe represents a substantial use.

Appellants argue that ESTs have real world value as seen from the "growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs." Brief, page 10. Since appellants fail to provide any suggestion on which use of ESTs this industry is premised on, we can only assume that appellants are referring to the potential usefulness of EST databases, clone sets or microarrays. Suffice it to say, the claims on appeal are not directed to EST databases, clone sets and/or microarrays. Again, it is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of claim 12 in such devices represents a substantial use.

Further, we understand appellants' position to be that a compound would be patentable if it was adequately described in the specification and was not disclosed or suggested in the prior art. This standard, however, is not the one

set by Congress, which requires that a patentable invention also be useful and fully enabled, nor is it the standard that has been consistently applied by the courts.

Not only is appellants' proposed utility standard contrary to controlling case law, but there are reasons to expect that it would hurt – rather than help – the microarray industry. Under appellants' standard, any naturally occurring gene, and fragments thereof, would be held to have patentable utility based on its use in generating expression data. The practical effect of this standard would be that making a microarray with, e.g., 1000 genes represented on it would require investigating the patent status of each oligonucleotide on the microarray. Not only that, but since appellants assert that their reasoning supports the utility of gene fragments, all of the subsequences of each of the genes or polypeptides would have to be checked to ensure that it was not the subject of someone else's patent.

For each of the genes (or fragments thereof) that was the subject of a patent claim held by someone else, a license would have to be negotiated – potentially thousands of such negotiations for the finished product. These transaction costs would have to be incurred for each new product that an aspiring microarray manufacturer wished to market. The industry gridlock likely to result from this scenario has been termed a “tragedy of the anticommons”:⁷

By conferring monopolies in discoveries, patents necessarily increase prices and restrict use—a cost society pays to motivate

⁷ Heller et al., “Can patents deter innovation? The anticommons in biomedical research,” *Science*, Vol. 280, pp. 698-701 (1998). Available online at www.sciencemag.org/cgi/content/full/280/5364/698.

invention and disclosure. The tragedy of the anticommons refers to the more complex obstacles that arise when a user needs access to multiple patented inputs to create a single useful product. Each upstream patent allows its owner to set up another tollbooth on the road to product development, adding to the cost and slowing the pace of downstream biomedical innovation.

Heller, page 698.

The Supreme Court has warned against allowing too many tollbooths on the road to innovation:

Patents . . . are meant to encourage invention by rewarding the inventor with the right, limited to a term of years fixed by the patent, to exclude others from the use of his invention. . . . But in rewarding useful invention, the "rights and welfare of the community must be fairly dealt with and effectually guarded." Kendall v. Winsor, 21 How. 322, 329 (1859).... To begin with, a genuine "invention" or "discovery" must be demonstrated "lest in the constant demand for new appliances the heavy hand of tribute be laid on each slight technological advance in an art."

Sears, Roebuck & Co. v. Stiffel Co., 376 U.S. 225, 230, 140 USPQ 524, 527 (1964).

The basic quid pro quo of the patent system requires disclosure of an invention having substantial utility. Appellants' disclosure in this case does not provide a specific benefit in currently available form, and therefore lacks the substantial utility required by 35 U.S.C. § 101.

For the foregoing reasons we affirm the rejection of claim 12 under 35 U.S.C. § 101. As discussed supra, claims 11 and 13-17 fall together with claim 12.

Enablement

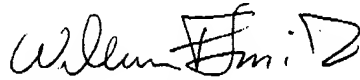
According to the examiner (Answer, page 4), "since the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." This rejection is simply a corollary of the finding of lack of utility. Appellants assert (Brief, page 12), this rejection should be reversed for the same reasons set forth in their arguments regarding the rejection under 35 U.S.C. § 101. Thus, our conclusion with respect to the § 101 issue will also apply to this aspect of the § 112 (enablement) issue. On this basis we affirm the rejection of claim 12 under the enablement provision of 35 U.S.C. § 112, first paragraph. As discussed supra, claims 11 and 13-17 fall together with claim 12.

Written description

Having disposed of all claims on appeal we do not reach the merits of the rejection under the written description provision of 35 U.S.C. § 112, first paragraph.

No time period for taking any subsequent action in connection with this
appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED



William F. Smith
Administrative Patent Judge



Donald E. Adams
Administrative Patent Judge



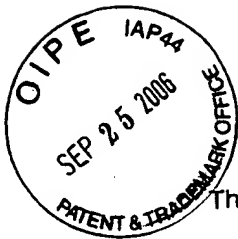
Eric Grimes
Administrative Patent Judge

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Appeal No. 2003-1744
Application No. 09/654,617

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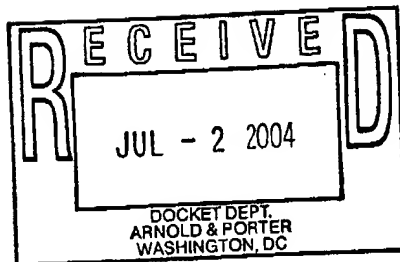
The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 35

UNITED STATES PATENT AND TRADEMARK OFFICE

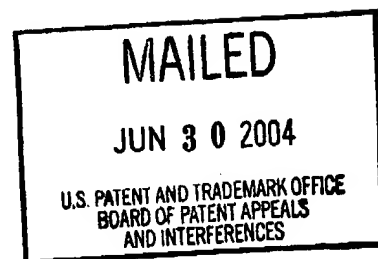
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte ANDREY A. BOUKHAROV,
YONGWEI CAO, DAVID K. KOVALIC,
JINGDONG LIU, JAMES MCININCH,
and WEI WU



Appeal No. 2003-1746
Application No. 09/620,392

HEARD June 8, 2004



Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-4, 6-9, and 16-20, all of the claims remaining. Claims 1 and 2 are representative and read as follows:

1. A substantially purified nucleic acid molecule having a nucleic acid sequence of SEQ ID NO:1 or complement thereof.
2. A substantially purified nucleic acid molecule comprising a fragment nucleic acid sequence having from about 50 to about 100 nucleotide residues; wherein said fragment nucleic acid sequence exhibits complete complementarity to a second nucleic acid molecule having a nucleic acid sequence of SEQ ID NO:1 or complement thereof.

The examiner does not rely on any prior art.

Claims 1-4, 6-9, and 16-20 stand rejected under 35 U.S.C. §§ 101 and 112, first paragraph, as lacking patentable utility.

Claims 1-4, 6-9, and 16-20 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description.¹

We affirm the utility rejections and reverse the description rejection.

Background

The subject matter of the present appeal is directed to "genomic DNA sequences from Oryza sativa (rice) plants." More specifically, the "invention provides a substantially purified nucleic acid molecule, the nucleic acid molecule capable of specifically hybridizing to a second nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:1 through SEQ ID NO:69652 or complements thereof or fragments of either."

According to the specification,

[a] subset of the nucleic acid molecules of the present invention includes nucleic acid molecules that are marker molecules. Another subset of the nucleic [acid] molecules of the present invention includes nucleic acid molecules that are promoters and/or regulatory elements. Another subset of the nucleic acid molecules of the present invention includes nucleic acid molecules that encode a gene or fragment thereof. Another subset of the nucleic acid molecules of the present invention encodes proteins or fragments of proteins.

Page 17. The specification provides no further guidance on which of the 69,652 disclosed sequences fall into each of these subsets.

¹ The examiner's statement of the rejection actually speaks in terms of lack of enablement. See the Examiner's Answer, page 5 (The claims "contain[] subject matter which lacks written description in the specification in such a way as to enable one skilled in the art . . . to make and/or use the invention."). The

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The originally filed claims encompassed all of the 69,652 disclosed sequences. See, e.g., original claim 1 (specification, page 55,578).² On June 18, 2001 (Paper No. 7), the examiner entered a restriction requirement into the record, requiring appellants to elect, inter alia, a single nucleotide sequence for examination on the merits. Paper No. 7, page 2. In response, Appellants elected SEQ ID NO:1. See Paper No. 8, received July 17, 2001.

The disclosure that relates specifically to SEQ ID NO:1 is found in the specification's Table 1 and reads as follows, in its entirety:

Seq No.	1	Seq. ID	OJ990503_31.9819.C2
Gene No.	1	Strand	-
Start	397	End	1864
Name	OJ990503_31.9819.C2.o1.gs	Method:	GENSCAN
Start	397	End	1238
GI	none	Score	.93
Exons	397. . 591, 879. . 1238		
Seq No.	1	Seq. ID	OJ990503_31.9819.C2
Gene No.	1	Strand	-
Start	397	End	1864
Name	OJ990503_31.9819.C2.o1.tm	Method:	TBLASTX:Maize
Start	1017	End	1864
GI	none	Score	150
Exons	1017. . 1250, 1018. . 1245, 1020. . 1247, 1243. . 1296, 1249. . 1296, 1377. . 1418, 1382. . 1420, 1532. . 1600, 1534. . 1596, 1706. . 1735, 1745. . 1864		

Page 104.

The specification sets forth a number of utilities for the claimed nucleic acid molecule which are characterized by the examiner as "[g]eneric to any rice nucleic acid

examiner's reasoning, however, explains the rejection in terms of lack of written description. We understand the rejection to be based on the written description requirement of § 112.

² The record is unclear as to precisely how many pages are in the specification. According to an error sheet generated by the USPTO's Office of Initial Patent Examination, the specification contains 68,885 pages; according to Appellants' page numbering, it contains only 55,580 pages. We have not attempted to resolve this discrepancy since it does not affect the issues on appeal.

sequences." Examiner's Answer, page 4. The examiner concluded that these uses do not establish patentable utility:

The claimed nucleic acids are not supported by a specific asserted utility because the disclosed uses of these nucleic acids are generally applicable to rice genomic nucleic acid. The specification states that the nucleic acid compounds are useful for gene mapping, marker assisted introgress[i]on of traits, physical mapping, etc. (page 9 and 49). All these possible uses are generic to any rice nucleic acid sequences. Further, the claimed nucleic acids are not supported by a substantial utility. . . . Identifying and studying the properties of a protein itself or the mechanisms in which the protein is involved does not define a "real world" context of use. Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds.

Examiner's Answer, pages 3-4.

In presenting their case on appeal, appellants focus on use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism, and their use as probes or as a source for primers. See the Appeal Brief, pages 6-13. According to Appellants, "they have disclosed nucleic acid molecules which, in their current form, provide at least one specific benefit to the public, for example, the ability to identify the presence or absence of a polymorphism in a population of rice plants." Id., page 4. Furthermore, appellants assert, "[t]he specification discloses that the claimed nucleic acid molecules can be used . . . to isolate nucleic acid molecules of other plants and organisms." Id., page 9.

1. Claim construction

The claims stand or fall together. Appeal Brief, page 3. Claim 2 is the broadest claim on appeal and we will consider it as representative.

As set forth above, claim 2 is directed to a "substantially purified" nucleic acid molecule that comprises a "fragment nucleic acid sequence having from about 50 to about 100 nucleotide residues"; where the 50-100 nucleotide sequence "exhibits complete complementarity to a second nucleic acid molecule having a nucleic acid sequence of SEQ ID NO:1" or its complement.

The specification defines "substantially purified" to mean

a molecule separated from substantially all other molecules normally associated with it in its native state. More preferably a substantially purified molecule is the predominant species present in a preparation. A substantially purified molecule may be greater than 60% free, preferably 75% free, more preferably 90% free, and most preferably 95% free from the other molecules (exclusive of solvent) present in the natural mixture. The term "substantially purified" is not intended to encompass molecules present in their native state.

Page 16, lines 12-18. As we understand the claimed invention, the use of the transitional term "comprising" does not allow for internal alterations (e.g., insertions or deletions) of the "fragment nucleic acid sequence" recited in the claim, but instead only allows for the addition of nucleotides or other molecules at either end of that sequence. Thus, claim 2 encompasses, inter alia, genes and fragments thereof, full or partial open reading frames, fusion constructs, and cDNAs.

Accordingly, we interpret claim 2 as directed to a nucleic acid molecule, separated from substantially all other molecules normally associated with it in its native state, that includes at least about 50 nucleotides that are completely complementary to a part of SEQ ID NO:1 or to the complement of a part of SEQ ID NO:1.

2. Utility

The starting point for determining whether the claimed nucleic acid molecules possess utility under 35 U.S.C. § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). At issue in Brenner was a claim to “a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced.” Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that “where a claimed process produces a known product it is not necessary to show utility for the product.” Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be “useful,” that “simple, everyday word can be pregnant with ambiguity when applied to the facts of life.” Id. at 529, 148 USPQ at 693. Thus,

[i]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the “new and useful” phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man’s grasp and where little or nothing is wholly beyond the pale of “utility”—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.³

³ The invention at issue in Brenner was a process, but the Court expressly noted that its holding “would apply equally to the patenting of the product produced by the process.” Id. at 535, 148 USPQ at 695-96.

The Court, finding “no specific assistance in the legislative materials underlying § 101,” based its analysis on “the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other.” Id. at 532, 148 USPQ at 695. The Court concluded that “[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.” Id. at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant’s argument that attenuating the requirement of utility “would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge.” The Court noted that, while there is value to encouraging disclosure, “a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development.” Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroidal research and in the application of steroidal materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the

compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are.” Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. “There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of ‘useful in research’ or ‘useful as building blocks of value to the researcher’ was recognized, and clearly rejected, by the Supreme Court” in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. “In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was ‘plastic-like.’” Id. at 1203, 26 USPQ2d at 1605. “Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility.” Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. Id. “[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there.” Id.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in cancer chemotherapy." Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were "relevant to the treatment of humans and [were] not to be disregarded," id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that "[it] is axiomatic that an invention cannot be considered 'useful,' in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious." Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court "perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question." Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by

“marshal[ing] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds ..., analogous to the benefit provided by the showing of an in vivo utility.” Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be “useful” is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every “use” that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy

§ 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best ... on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

With these principles in mind we turn to the issues at hand. Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal; i.e., identification and detection of polymorphisms and use as probes or as a source for primers. We will focus on these asserted utilities first.

a. Polymorphisms

This utility is discussed at pages 57-64 of the specification in terms of what polymorphisms are and how one would go about determining the existence of a polymorphism. The discussion in this portion of the specification, however, is not specific to SEQ ID NO:1. To the contrary, according to the specification, "[t]he [69,652] nucleic acid molecules of the present invention can be used to identify polymorphisms. In one embodiment, one or more of the nucleic acid molecules . . . may be employed as a marker nucleic acid molecule to identify . . . polymorphism(s)." Page 57. The specification does not explain why any particular one of the 69,652 nucleic acid molecules disclosed in the specification, or more specifically SEQ ID NO:1, would in fact be useful in detecting polymorphisms.

Rather, Appellants argue that "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." Appeal Brief, page 9. In other words, Appellants' position is that a rice genomic DNA by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by a nucleotide sequence, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage. As the examiner explains,

[a] "polymorphism" is a collective concept defined by at least two variants (or alleles) found within members of a species collectively. Thus, one detects the presence of a polymorphism by analyzing multiple members of the species, i.e. analyzing a population. . . . The specification fails to disclose a specific and substantial utility for the claimed invention in the capacity of detecting polymorphisms, because it does not disclose whether the claimed nucleic acid molecules can, in fact, be used to detect any polymorphism whatsoever. . . .

The specification generally teaches using the claimed polynucleotides to identify a polymorphism, but fails to teach that a polymorphism could in fact be detected, or a specific polymorphism that could be detected. The specification generally teaches using a polymorphism, detectable with the claimed nucleic acid molecules, as a molecular marker for a linked trait of interest, but fails to teach either the polymorphism or the trait of interest.

Examiner's Answer, pages 12-13. In contrast, at the other end of the "utility spectrum" would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene represented by the claimed sequence has in the development and/or phenotype of the plant. Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the gene and its role in the plant's development and/or phenotype lies the line that defines "substantial utility." We need not draw the line or further define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.

b. Probes or source of primers

Appellants argue that the "specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms." Appeal Brief, page 9. That may be true, but it does not show the patentable utility of the claimed nucleic acids, because the nucleic acids isolated from other plants have no apparent, substantial use. Again, the present specification does not attribute any property in terms of plant trait or phenotype to SEQ ID NO:1. In the absence of such information, nucleic acids from other plants that hybridize to the claimed nucleic acids themselves lack substantial utility. Thus, the use of the claimed nucleic acids to isolate such nucleic acids does not represent a substantial utility.

Appellants also assert that the claimed nucleic acid molecules may be used in a "chromosome walk." Appeal Brief, pages 10-11. According to Appellants,

[t]he claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter that is active in Oryza sativa. A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter. Furthermore, even if a random nucleic acid provided a better starting point than the claimed nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules.

Id., page 10. As we understand it, Appellants' argument is that the claimed nucleic acids may be useful in searching for promoters that are active in rice tissues.

The specification, however, fails to demonstrate that the nucleic acid represented by SEQ ID NO:1 would be useful in obtaining a successful result from such a search.

The specification states that "[a]nother class of agents of the present invention are nucleic acid molecules having promoter regions or partial promoter regions within SEQ ID NO:1 through SEQ ID NO:69652." Page 27.

Promoters . . . include, but are not limited to, oxygen responsive cis elements . . . , light regulatory elements . . . , elements responsive to gibberellin . . . , elements responsive to abscisic acid . . . , elements similar to abscisic acid responsive elements . . . , auxin responsive elements . . . , ethylene responsive cis elements . . . , sucrose responsive elements . . . , heat shock response elements . . . , Elicitor responsive elements . . . , drought responsive elements . . . , light-independent regulatory elements . . . , ACGT elements . . . , [and] prolamin box elements.

Pages 28-32.

The specification does not provide any expectation of successfully using any of the 69,652 nucleic acid molecules disclosed in the specification, or more specifically the nucleic acid of SEQ ID NO:1, to isolate any of the promoters exhaustively listed in the specification, or any other promoter. Even if SEQ ID NO:1 represents a gene that is expressed in rice tissue, the specification provides no characterization of its expression (e.g., amount expressed, timing of expression, tissues in which or conditions under which it is expressed) that would suggest a utility for its putative promoter.

It is true, as Appellants argue, that “[a]n invention may be ‘less effective than existing devices but nevertheless meet the statutory criteria for patentability.’” Appeal Brief, page 11. However, with Appellants’ claimed invention, there is no evidence or expectation that the claimed nucleic acid molecules would be “effective” at all. An invention does not have utility sufficient to satisfy § 101 until it is “refined and developed” to the point of providing a specific benefit in currently available form. See Brenner, 383 U.S. at 534, 148 USPQ at 695.

Appellants argue that the claimed nucleotide sequences are no less useful just because other nucleic acids can also be used to isolate promoters. See the Appeal Brief, page 10: “[T]he Examiner suggests that the asserted utilities are legally

insufficient simply because other molecules can be used for the same purpose. This position is wrong as a matter of law – there is no requirement of exclusive utility in the patent law.”

This argument is not persuasive. Appellants have not been asked to identify a utility that is unique, i.e., not shared by any other compounds or compositions. Rather, Appellants have been required to identify a utility that is specific to the invention claimed, as opposed to one that would apply regardless of the specific properties of the claimed invention. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695 (An invention does not have utility sufficient to satisfy § 101 until it is “refined and developed” to the point of providing a specific benefit in currently available form.).

An invention certainly can have a utility that is shared by other compounds or compositions. Take, for example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful as analgesics.

On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

Here, Appellants argue that asserted "chromosome walking" utility would support patentability even if the claimed nucleic acid molecule was less useful for this purpose than a totally random nucleotide sequence. Appeal Brief, page 10 ("[E]ven if a random nucleic acid provided a better starting point than the claimed nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules."). Clearly, the asserted utility is not based on the specific properties of the claimed nucleic acid molecules.

c. Other arguments

Appellants argue that the specification "discloses additional utilities for the claimed nucleic acid molecules, including introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for compounds such as a herbicide." Appeal Brief, page 6 (footnote omitted). Specifically, Appellants argue (id.) that "a compound can be provided to both an antisense plant and a control plant (no antisense) and the effect of the compound on the plant can be monitored." Appellants analogize this proposed procedure to a "cell-based assay" which, they assert, has a "legally sufficient utility." Id.

Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. The portions of the specification cited in support of this argument (pages 69 and 86-88) indicate that the nucleic acid molecule must be introduced into a plant cell and transcribed using an appropriate promoter to result in either expression of the protein or suppression of an endogenous protein. The specification does not indicate that such a method is feasible when the nucleic acid to

be used is uncharacterized as here. Such a use does not provide a specific or substantial benefit in currently available form.

Appellants also argue that the claimed nucleic acids are useful to measure the level of mRNA in a sample through use of microarray technology and use as molecular markers. Appeal Brief, page 7. In regard to microarrays, Appellants argue (*id.*, n.3) that it is "standard practice" to screen populations of nucleic acids with EST sequences without characterizing each and every target mRNA. We find that this asserted utility of the claimed nucleic acid—as one component of an assay for monitoring gene expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form.

We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid depicted in SEQ ID NO:1. However, the specification provides no guidance that would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification provides no guidance regarding what the SEQ ID NO:1-specific information derived from a gene expression experiment would mean. As the examiner points out, "further experimentation is required to identify a 'real world use.' . . . A positive result to such a screen requires further experimentation to determine what, if anything, such a change means." Examiner's Answer, pages 8-9.

To highlight the examiner's assertion, suppose, for example, that a researcher found that SEQ ID NO:1 expression was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be

able to determine whether that result is meaningful. Maybe the meaning in a change in SEQ ID NO:1 expression would depend on other factors, but again the specification provides no hint as to what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), or the degree of increase? The specification provides no guidance as to how to interpret the results that might be seen using SEQ ID NO:1 in a gene expression assay.

In effect, Appellants' position is that the claimed nucleic acids are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the present case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, Appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, based on their use in gene expression assays, because the specification does not disclose how to use gene expression data pertaining to SEQ ID NO:1.

In addition, assuming arguendo that a generic gene expression assay—one based on monitoring expression of a collection of uncharacterized nucleic acids—would

provide a useful tool for, e.g., drug discovery, it does not follow that each of the nucleic acids in the assay necessarily has patentable utility. Although each nucleic acid in the assay contributes to the data generated by the assay overall, the contribution of a single nucleic acid—its data point—is only a tiny contribution to the overall picture.

The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently available form. Providing a single data point among thousands, even if the thousands of data points collectively are useful, does not meet this standard.

We also conclude that § 101's utility requirement is not satisfied by Appellants' assertion that the claimed nucleic acid molecules are useful as molecular markers or probes. Again, using one of the claimed nucleic acids as a molecular marker or probe to hybridize to part of a rice chromosome merely generates a single, uncharacterized data point that is useful only when combined with thousands of other data points. For the reasons discussed above in regard to gene expression assays, such uses do not represent "substantial" utility, as required by Brenner.

Appellants argue that ESTs (and presumably other uncharacterized nucleic acids – the claims on appeal are not directed to ESTs) have real world value as seen from the "growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs." Appeal Brief, page 12. Since Appellants fail to provide any

suggestion of which use of ESTs this industry is premised on, we can only assume that Appellants are referring to the potential usefulness of EST databases, clone sets, or microarrays. The claims on appeal, however, are not directed to EST databases, clone sets, or microarrays, but to individual, uncharacterized nucleic acids. Again, we do not agree that the one data point which may be provided by using the uncharacterized nucleic acid molecules of the claims in such devices represents a substantial use.

In addition, it is reasonable to expect that the rule Appellants proffer – that uncharacterized nucleic acids are individually patentable because they are useful in gene expression assays – would hurt, rather than help, what they characterize as a “multi-million dollar industry in the United States premised on the usefulness of ESTs.” Under Appellants’ standard, any uncharacterized nucleic acid from most (if not all) organisms would be held to have patentable utility based on its use in generating gene expression data.⁴ The practical effect of this standard would be that making a microarray with, e.g., 1000 genes represented on it would require investigating all of the DNA sequences on the microarray to ensure that they were not the subject of someone else’s patent.

For each of the DNAs that was the subject of a patent claim held by someone else, a license would have to be negotiated – potentially thousands of such negotiations for the finished product. These transaction costs would have to be incurred for each

⁴ We can take judicial notice of the fact that organisms are of interest for many different reasons, such that gene expression assays could conceivably be used in their research. Humans, of course, are of interest in medical research. Other organisms are of interest to researchers because they have been historically well-studied (e.g., yeast, Arabidopsis, Drosophila), or because they are used as animal models for testing pharmaceuticals (e.g., mice, chimpanzees, rabbits), or because they are commercially valuable (e.g., pigs, corn, tomatoes), or because they are pests (e.g., Fusarium, ragweed, corn borers, zebra mussels), or because they are pathogens (e.g., Candida, various bacteria, tapeworms).

new product that an aspiring microarray manufacturer wished to market. The industry gridlock likely to result from this scenario has been termed a "tragedy of the anticommons".⁵

By conferring monopolies in discoveries, patents necessarily increase prices and restrict use—a cost society pays to motivate invention and disclosure. The tragedy of the anticommons refers to the more complex obstacles that arise when a user needs access to multiple patented inputs to create a single useful product. Each upstream patent allows its owner to set up another tollbooth on the road to product development, adding to the cost and slowing the pace of downstream biomedical innovation.

Heller, page 698.

The Supreme Court has warned against allowing too many tollbooths on the road to innovation:

Patents . . . are meant to encourage invention by rewarding the inventor with the right, limited to a term of years fixed by the patent, to exclude others from the use of his invention. . . . But in rewarding useful invention, the "rights and welfare of the community must be fairly dealt with and effectually guarded." Kendall v. Winsor, 21 How. 322, 329 (1859). . . . To begin with, a genuine "invention" or "discovery" must be demonstrated "lest in the constant demand for new appliances the heavy hand of tribute be laid on each slight technological advance in an art."

Sears, Roebuck & Co. v. Stiffel Co., 376 U.S. 225, 230, 140 USPQ 524, 527 (1964).

The basic quid pro quo of the patent system requires disclosure of an invention having substantial utility. Appellants' disclosure in this case does not provide a specific benefit in currently available form, and therefore lacks the substantial utility required by 35 U.S.C. § 101. We therefore affirm the rejection of claim 2 under 35 U.S.C. § 101. Claims 1, 3, 4, 6-9, and 16-20 fall with claim 2.

⁵ Heller et al., "Can patents deter innovation? The anticommons in biomedical research," Science, Vol. 280, pp. 698-701 (1998). Available online at www.sciencemag.org/cgi/content/full/280/5364/698.

3. Enablement

The examiner rejected claims 1-4, 6-9, and 16-20 under 35 U.S.C. § 112, first paragraph, on the basis that "since the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." Examiner's Answer, page 4. This rejection is simply a corollary of the finding of lack of utility.

Appellants argue that "[t]his rejection . . . has been overcome by the arguments stated above regarding utility." Appeal Brief, page 14. We do not agree that Appellants' arguments overcome the rejection for lack of utility. Thus, our conclusion with respect to the § 101 issue also applies to the nonenablement rejection. On this basis we affirm the rejection of claims 1-4, 6-9, and 16-20 under the enablement provision of 35 U.S.C. § 112, first paragraph.

4. Written description

The examiner rejected claims 1-4, 6-9, and 16-20 under 35 U.S.C. § 112, first paragraph, for lack of adequate written description, reasoning that

[c]laims 1-4, 6-9, and 16-20 are directed to nucleic acids comprising . . . SEQ ID NO:1, or fragments thereof. . . . [G]iven the broad scope of the claims, they are drawn to a genus: any polynucleotide or nucleic acid that minimally contains the sequence of the claimed SEQ ID NO, or a fragment thereof, including any full length gene which contains the sequence. . . . Since the claimed genus encompasses species yet to be discovered, the mere disclosure of a species: sequence of the claimed SEQ ID NO, does not provide an adequate description of the claimed genus. . . . With the exception of SEQ ID NO:1, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotide.

Examiner's Answer, page 5.

As we understand it, the basis of the examiner's rejection is that because of the transitional phrase "comprising", the claims encompass a large genus of nucleic acid molecules which are not adequately described by SEQ ID NO:1. See the Examiner's Answer, pages 18-20. Apparently, the examiner is of the opinion that the claimed invention should be limited to the nucleic acid molecules set forth in SEQ ID NO:1.

In response, Appellants argue that "[t]he fact that the claims at issue are intended to cover molecules that include the recited sequences joined with additional sequences . . . does not mean that Applicants were any less in possession of the claimed nucleic acid molecules." Appeal Brief, pages 15-16.

We have interpreted claim 2 to allow for the addition of nucleotides or other molecules at either end of the recited nucleotide sequences, but not to allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequence SEQ ID NO:1. See pages 4-5, supra. We agree with Appellants that the claims, as we have interpreted them, are supported by an adequate written description in the specification. The fact that the claimed nucleic acid molecules may have other molecules attached to either or both of their 5' or 3' ends does not diminish Appellants' adequate written description of the nucleic acids molecules with at least part of the sequence set forth in SEQ ID NO:1, as claimed.

Accordingly, we reverse the rejection of claims 1-4, 6-9, and 16-20 for lack of adequate written description.

Summary

Although we reverse the examiner's rejection for lack of adequate written description, we affirm the rejection of claims 1-4, 6-9, and 16-20 for lack of patentable utility.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED


WILLIAM F. SMITH
Administrative Patent Judge


DONALD E. ADAMS
Administrative Patent Judge


ERIC GRIMES
Administrative Patent Judge

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Application No. 09/620,392

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The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 22

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

(15768)
Ex parte SCOTT E. ANDERSEN and JAMES D. MASUCCI

Appeal to C.A.F.C.
Appeal No. 2003-1137
Application No. 09/540,232
Docketed
Due Date 8/30/04
Initial uo

ON BRIEF



Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

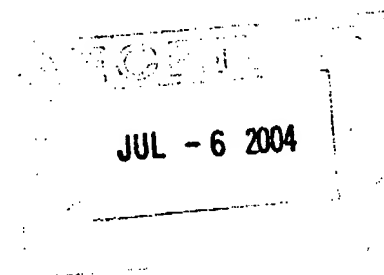
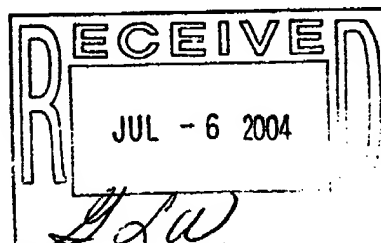
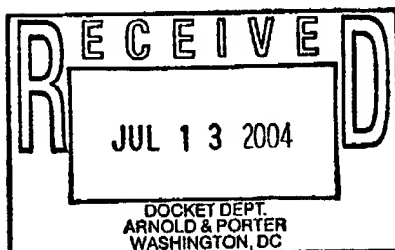
GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1 and 2, the only claims remaining. The claims read as follows:

1. A substantially purified nucleic acid molecule that encodes a plant protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:78, SEQ ID NO:93, SEQ ID NO:340, SEQ ID NO:1965, SEQ ID NO:1985, SEQ ID NO:1991, SEQ ID NO:1993, SEQ ID NO:4047, and SEQ ID NO:5683.

2. The substantially purified nucleic acid molecule according to claim 1, wherein said plant protein or fragment thereof is a lily protein or fragment thereof.



The examiner does not rely on any prior art.

Claims 1 and 2 stand rejected under 35 U.S.C. §§ 101 and 112, first paragraph, as lacking patentable utility.

Claims 1 and 2 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description in the specification.

We affirm the utility rejections and reverse the description rejection.

Background

The subject matter of the present appeal is directed to expressed sequence tags. "Expressed sequence tags, or ESTs, are short sequences of randomly selected clones from a cDNA (or complementary DNA) library which are representative of the cDNA inserts of these randomly selected clones." Specification, page 1.

As set forth at page 9 of the specification, "[t]he present invention provides a substantially purified nucleic acid molecule that encodes a lily protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:1 through SEQ ID NO:6167." The specification discloses that these ESTs were obtained from cDNA libraries prepared from asiatic lily early ovary or late ovule tissue. Pages 84-85.

The originally filed claims encompassed all of the 6167 disclosed sequences. On January 9, 2001 (Paper No. 4), the examiner entered a restriction requirement into the record, requiring appellants to elect, inter alia, up to ten nucleotide sequences for examination on the merits. Paper No. 4, page 2. In response, appellants elected SEQ ID NOs 78, 93, 340, 1954, 1965, 1985, 1991, 1993, 4047, and 5683. See Paper No. 5,

received Feb. 9, 2001. During prosecution, SEQ ID NO:1954 was deleted from the claims. See Paper No. 10, received Dec. 13, 2001.

The specification sets forth a number of utilities for the claimed nucleic acid molecules which are characterized by the examiner as "[g]eneral uses . . . includ[ing] acquiring genes, identifying polymorphisms, determining plant traits, and DNA mapping." Examiner's Answer, page 4. The examiner concluded that these uses do not establish patentable utility:

None of these [uses are] considered to be specific and substantial in view of the limited information provided in the specification. No plant traits are attributed to any SEQ ID NO. No complete gene is disclosed for any SEQ ID NO. No DNA maps or chromosomal locations are identified. No polymorphisms are identified. The specification does not disclose how a polymorphism would be recognized by those of ordinary skill in the art given the incomplete sequences disclosed.

Examiner's Answer, page 4.

In presenting their case on appeal, appellants focus on use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism, and their use as probes or as a source for primers. See the Appeal Brief, pages 6-13. According to Appellants, "they have disclosed nucleic acid molecules which, in their current form, provide at least one specific benefit to the public, e.g., the ability to identify the presence or absence of a polymorphism in a population of lily plants." Id., page 3. Furthermore, appellants assert, "[t]he specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms." Id., page 8.

Discussion

1. Claim construction

As set forth above, claim 1 is directed to a "substantially purified nucleic acid molecule that encodes a plant protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:78, SEQ ID NO:93, SEQ ID NO:340, SEQ ID NO:1965, SEQ ID NO:1985, SEQ ID NO:1991, SEQ ID NO:1993, SEQ ID NO:4047, and SEQ ID NO:5683." The specification defines "substantially purified" to mean

a molecule separated from substantially all other molecules normally associated with it in its native state. More preferably a substantially purified molecule is the predominant species present in a preparation. A substantially purified molecule may be greater than 60% free, preferably 75% free, more preferably 90% free, and most preferably 95% free from the other molecules (exclusive of solvent) present in the natural mixture. The term "substantially purified" is not intended to encompass molecules present in their native state.

Page 16, lines 12-18. As we understand the claimed invention, the use of the transitional term "comprising" does not allow for internal alterations (e.g., insertions or deletions) of the nucleotide sequences set forth in the recited SEQ ID NOs, but instead only allows for the addition of nucleotides or other molecules at either end of the nucleotide sequences of the recited SEQ ID NOs. Thus, claim 1 encompasses, inter alia, genes, full open reading frames, fusion constructs, and cDNAs.

The preamble of claim 1 also recites that the claimed nucleic acid "encodes a plant protein or fragment thereof." This phrase, however, merely recites an inherent function expected for the nucleotide sequences of the recited SEQ ID NOs; since the recited sequences were isolated as ESTs from lily tissue, they would be expected to

encode (parts of) lily proteins. Since the introductory phrase does not further limit the invention defined by the body of the claim, it is irrelevant to construction of the claim.

See IMS Technology, Inc. v. Haas Automation, Inc., 206 F.3d 1422, 1434, 54 USPQ2d 1129, 1137 (Fed. Cir. 2000) ("If the preamble adds no limitations to those in the body of the claim, the preamble is not itself a claim limitation and is irrelevant to proper construction of the claim.").

Accordingly, we interpret claim 1 as directed to a nucleic acid molecule, separated from substantially all other molecules normally associated with it in its native state, comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:78, SEQ ID NO:93, SEQ ID NO:340, SEQ ID NO:1965, SEQ ID NO:1985, SEQ ID NO:1991, SEQ ID NO:1993, SEQ ID NO:4047, and SEQ ID NO:5683, with or without any preceding or trailing nucleotides or other molecules.

2. Utility

The starting point for determining whether the claimed nucleic acid molecules possess utility under 35 U.S.C. § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). At issue in Brenner was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that "where a claimed process produces a known product it is not necessary to show utility for the product." Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be “useful,” that “simple, everyday word can be pregnant with ambiguity when applied to the facts of life.” Id. at 529, 148 USPQ at 693. Thus,

[i]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the “new and useful” phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man’s grasp and where little or nothing is wholly beyond the pale of “utility”—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.¹

The Court, finding “no specific assistance in the legislative materials underlying § 101,” based its analysis on “the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other.” Id. at 532, 148 USPQ at 695. The Court concluded that “[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.” Id. at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant’s argument that attenuating the requirement of utility “would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge.” The Court noted that, while there

is value to encouraging disclosure, "a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroidal research and in the application of steroidal materials to

¹ The invention at issue in Brenner was a process, but the Court expressly noted that its holding "would apply equally to the patenting of the product produced by the process." Id. at 535, 148 USPQ at 695-96.

veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only

that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" Id. at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. Id. "[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there." Id.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in cancer chemotherapy." Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were "relevant to the treatment of humans and [were] not to be disregarded," id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that “[it] is axiomatic that an invention cannot be considered ‘useful,’ in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious.” Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court “perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question.” Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by “marshal[ling] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds ..., analogous to the benefit provided by the showing of an in vivo utility.” Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at

1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best ... on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

With these principles in mind we turn to the issues at hand. Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal; i.e., identification and detection of polymorphisms and use as probes or as a source for primers. We will focus on these asserted utilities first.

a. Polymorphisms

This utility is discussed at pages 38-45 of the specification in terms of what polymorphisms are and how one would go about determining the existence of a polymorphism. The discussion in this portion of the specification, however, is not specific to the nucleotide molecules depicted in any of the SEQ ID NOs recited in claim 1. To the contrary, according to the specification, "one or more of the [6167] EST nucleic acid molecules (or a sub-fragment thereof) may be employed as a marker nucleic acid molecule to identify . . . polymorphism(s)." Page 35, lines 25-26. The specification does not explain why any of the 6167 nucleic acid molecules disclosed in the specification, or more specifically the nine nucleotide molecules depicted in SEQ ID NOs 78, 93, 340, 1965, 1985, 1991, 1993, 4047, and 5683, would in fact be useful in detecting polymorphisms.

Rather, Appellants argue that "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." Appeal Brief, page 8. In other words, Appellants' position is that an EST by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by an EST, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage. As the examiner explains,

[a] "polymorphism" is a collective concept defined by at least two variants (or alleles) found within members of a species collectively. Thus, one detects the presence of a polymorphism by analyzing multiple members of the species, i.e. analyzing a population. . . . The specification fails to disclose a specific and substantial utility for the claimed invention in the capacity of detecting polymorphisms, because it does not disclose whether the claimed nucleic acid molecules can, in fact, be used to detect any polymorphism whatsoever. . . .

The specification generally teaches using the claimed polynucleotides to identify a polymorphism, but fails to teach that a polymorphism could in fact be detected, or a specific polymorphism that could be detected. The specification generally teaches using a polymorphism, detectable with the claimed nucleic acid molecules, as a molecular marker for a linked trait of interest, but fails to teach either the polymorphism or the trait of interest.

Examiner's Answer, pages 11-12. In contrast, at the other end of the "utility spectrum" would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene from which the EST is derived has in the development and/or phenotype of the plant. Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the gene

and its role in the plant's development and/or phenotype lies the line that defines "substantial utility." We need not draw the line or further define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.

b. Probes or source of primers

Appellants argue that the "specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms." Appeal Brief, page 8. That may be true, but it does not show the patentable utility of the claimed nucleic acids, because the nucleic acids isolated from other plants have no apparent, substantial use. Again, the present specification does not attribute any property in terms of plant trait or phenotype to any of the nucleic acid molecules set forth in the SEQ ID NOs recited in claim 1. In the absence of such information, nucleic acids from other plants that hybridize to the claimed nucleic acids themselves lack substantial utility. Thus, the use of the claimed nucleic acids to isolate such nucleic acids does not represent a substantial utility.

Appellants also assert that the claimed nucleic acid molecules may be used in a "chromosome walk." Appeal Brief, pages 9-10. According to Appellants,

[t]he claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter that is active in ovary tissues at early and late stages of development. Isolation of such a promoter would be desirable and particularly useful because it allows expression of proteins at important developmental states, including proteins that provide increased reproductive ability. Because the claimed nucleic acid molecules were isolated from ovary tissue, they provide an appropriate starting point for isolating a promoter active in ovary tissue. A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter.

Id., page 10. As we understand it, Appellants' argument is that the claimed ESTs may be useful in searching for promoters that are only active in ovary tissue. The specification, however, fails to demonstrate that any of the nucleic acid molecules set forth in the SEQ ID NOs recited in claim 1 would be useful in obtaining a successful result from such a search. The specification states that

[t]he [6167] nucleic acid molecules of the present invention may be used to isolate promoters of tissue enhanced[,] tissue specific, cell-specific, cell-type, developmentally or environmentally regulated expression profiles. Isolation and functional analysis of the 5' flanking promoter sequences of these genes from genomic libraries, for example, using genomic screening methods and PCR techniques would result in the isolation of useful promoters and transcriptional regulatory elements.

The specification does not provide any expectation of successfully using any of the 6167 nucleic acid molecules disclosed in the specification, or more specifically the nine nucleic acid molecules depicted in the SEQ ID NOs of claim 1, to isolate promoters of tissue-enhanced, tissue-specific, cell-specific, cell-type, developmentally or environmentally regulated expression profiles.

Furthermore, notwithstanding Appellants' assertion (Brief, page 10), there is no evidence on this record that any of the nucleic acid molecules recited in claim 1 are expressed in a tissue- or cell-type specific manner, or are developmentally or environmentally regulated. In this regard, we note that the claimed nucleic acid molecules were isolated from the cDNA libraries LIB3102 and LIB3103. Specification, pages 84-85. There is no evidence on this record that either of these libraries is a subtractive cDNA library, wherein nucleic acid molecules from other lily tissue, or from other developmental stages, was subtracted (removed) from the library. Thus, the cDNAs in the libraries LIB3102 and LIB3103 would be expected to include genes that

are expressed in a variety of lily tissues (e.g., genes involved in basic cell metabolism, synthesis of amino acids and other cellular components, and genes encoding ubiquitous structural proteins).

In our opinion, the claimed nucleic acid molecules having the sequences identified as SEQ ID NOs 78, 93, 340, 1965, 1985, 1991, 1993, 4047, and 5683, represent nine randomly selected nucleic acid molecules isolated from lily ovary tissue. Despite Appellants' assertion to the contrary, there is no reasonable expectation that any of the claimed nucleic acid molecules would be capable of isolating a promoter that was only active in ovary tissue. As Appellants recognize (Brief, page 10), "[a] random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter" compared to a nucleic acid molecule that is known to be specifically associated with this stage of plant development.

It is true, as Appellants argue, that "[a]n invention may be 'less effective than existing devices but nevertheless meet the statutory criteria for patentability.'" Appeal Brief, page 10. However, with Appellants' claimed invention, there is no evidence or expectation that the claimed nucleic acid molecules would be "effective" at all. An invention does not have utility sufficient to satisfy § 101 until it is "refined and developed" to the point of providing a specific benefit in currently available form. See Brenner, 383 U.S. at 534, 148 USPQ at 695.

Appellants argue that the claimed nucleotide sequences are no less useful just because other nucleic acids can also be used to isolate promoters. See the Appeal Brief, page 9: "[T]he Examiner suggests that the asserted utilities are legally insufficient

simply because other molecules can be used for the same purpose. This position is wrong as a matter of law – there is no requirement of exclusive utility in the patent law.”

This argument is not persuasive. Appellants have never been asked to identify a utility that is unique, i.e., not shared by any other compounds or compositions. Rather, Appellants have been required to identify a utility that is specific to the invention claimed, as opposed to one that would apply regardless of the specific properties of the claimed invention. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695 (An invention does not have utility sufficient to satisfy § 101 until it is “refined and developed” to the point of providing a specific benefit in currently available form.).

An invention certainly can have a utility that is shared by other compounds or compositions. Take, for example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful as analgesics.

On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

Here, Appellants argue that asserted “chromosome walking” utility would support patentability even if the claimed nucleic acid molecules were less useful for this purpose

than a totally random nucleotide sequence. Appeal Brief, page 10 ("[E]ven if a random nucleic acid provided a better starting point than the claimed nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules."). Clearly, the asserted utility is not based on the specific properties of the claimed nucleic acid molecules.

c. Other arguments

Appellants argue that the specification "discloses additional utilities for the claimed nucleic acid molecules including introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for compounds such as a herbicide." Appeal Brief, page 6. Specifically, Appellants argue (id.) that "a compound can be provided to both an antisense plant and a control plant (no antisense) and the effect of the compound on the plant can be monitored." Appellants analogize this proposed procedure to a "cell-based assay" which, they assert, has a "legally sufficient utility." Id.

Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. The portion of the specification cited in support of this argument (pages 75-78) indicates that the nucleic acid molecule must be introduced into a plant cell and transcribed using an appropriate promoter to result in the suppression of an endogenous protein. The specification does not indicate that such a method is feasible when the nucleic acid to be used is uncharacterized as here. Such a use does not provide a specific or substantial benefit in currently available form.

Appellants also argue that the claimed nucleic acids are useful to measure the level of mRNA in a sample through use of microarray technology and use as molecular

markers. Appeal Brief, page 6. In regard to microarrays, Appellants argue (*id.*, n.2) that it is “standard practice” to screen populations of nucleic acids with EST sequences without characterizing each and every target mRNA. We find that this asserted utility of the claimed nucleic acid—as one component of an assay for monitoring gene expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form. We accept, for argument’s sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid depicted in, e.g., SEQ ID NO:78. However, the specification provides no guidance that would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification provides no guidance regarding what the SEQ ID NO:78-specific information derived from a gene expression experiment would mean. As the examiner points out, “further experimentation is required to identify a ‘real world use.’ . . . A positive result to such a screen requires further experimentation to determine what, if anything, such a change means.” Examiner’s Answer, page 9.

To highlight the examiner’s assertion, suppose, for example, that a researcher found that SEQ ID NO:78 expression was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. Maybe the meaning in a change in SEQ ID NO:78 expression would depend on other factors, but again the specification provides no hint as to what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), or the degree of increase? The specification provides

The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently available form. Providing a single data point among thousands, even if the thousands of data points collectively are useful, does not meet this standard.

We also conclude that § 101's utility requirement is not satisfied by Appellants' assertion that the claimed nucleic acid molecules are useful as molecular markers or probes. Again, using one of the claimed nucleic acids as a molecular marker or probe to hybridize to part of a lily chromosome merely generates a single, uncharacterized data point that is useful only when combined with thousands of other data points. For the reasons discussed above in regard to gene expression assays, such uses do not represent "substantial" utility, as required by Brenner.

Appellants argue that ESTs have real world value as seen from the "growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs." Appeal Brief, page 12. Since Appellants fail to provide any suggestion of which use of ESTs this industry is premised on, we can only assume that Appellants are referring to the potential usefulness of EST databases, clone sets, or microarrays. The claims on appeal, however, are not directed to EST databases, clone sets, or microarrays, but to individual, uncharacterized ESTs. Again, we do not agree that the one data point which

may be provided by using the uncharacterized nucleic acid molecules of claim 1 in such devices represents a substantial use.

In addition, it is reasonable to expect that the rule Appellants proffer – that ESTs are individually patentable because they are useful in gene expression assays – would hurt, rather than help, what they characterize as a “multi-million dollar industry in the United States premised on the usefulness of ESTs.” Under Appellants’ standard, any EST from most (if not all) organisms would be held to have patentable utility based on its use in generating gene expression data.² The practical effect of this standard would be that making a microarray with, e.g., 1000 genes represented on it would require investigating all of the DNA sequences on the microarray to ensure that they were not the subject of someone else’s patent.

For each of the DNAs that was the subject of a patent claim held by someone else, a license would have to be negotiated – potentially thousands of such negotiations for the finished product. These transaction costs would have to be incurred for each new product that an aspiring microarray manufacturer wished to market. The industry gridlock likely to result from this scenario has been termed a “tragedy of the anticommons”:³

By conferring monopolies in discoveries, patents necessarily increase prices and restrict use—a cost society pays to motivate invention and disclosure. The tragedy of the anticommons refers to the more complex

² We can take judicial notice of the fact that organisms are of interest for many different reasons, such that gene expression assays could conceivably be used in their research. Humans, of course, are of interest in medical research. Other organisms are of interest to researchers because they have been historically well-studied (e.g., yeast, Arabidopsis, Drosophila), or because they are used as animal models for testing pharmaceuticals (e.g., mice, chimpanzees, rabbits), or because they are commercially valuable (e.g., pigs, corn, tomatoes), or because they are pests (e.g., Fusarium, ragweed, corn borers, zebra mussels), or because they are pathogens (e.g., Candida, various bacteria, tapeworms).

³ Heller et al., “Can patents deter innovation? The anticommons in biomedical research,” Science, Vol. 280, pp. 698-701 (1998). Available online at www.sciencemag.org/cgi/content/full/280/5364/698.

obstacles that arise when a user needs access to multiple patented inputs to create a single useful product. Each upstream patent allows its owner to set up another tollbooth on the road to product development, adding to the cost and slowing the pace of downstream biomedical innovation.

Heller, page 698.

The Supreme Court has warned against allowing too many tollbooths on the road to innovation:

Patents . . . are meant to encourage invention by rewarding the inventor with the right, limited to a term of years fixed by the patent, to exclude others from the use of his invention. . . . But in rewarding useful invention, the "rights and welfare of the community must be fairly dealt with and effectually guarded." Kendall v. Winsor, 21 How. 322, 329 (1859). . . . To begin with, a genuine "invention" or "discovery" must be demonstrated "lest in the constant demand for new appliances the heavy hand of tribute be laid on each slight technological advance in an art."

Sears, Roebuck & Co. v. Stiffel Co., 376 U.S. 225, 230, 140 USPQ 524, 527 (1964).

The basic quid pro quo of the patent system requires disclosure of an invention having substantial utility. Appellants' disclosure in this case does not provide a specific benefit in currently available form, and therefore lacks the substantial utility required by 35 U.S.C. § 101. We therefore affirm the rejection of claim 1 under 35 U.S.C. § 101.

Claim 2 falls with claim 1. See the Appeal Brief, page 3.

3. Enablement

The examiner rejected claims 1 and 2 under 35 U.S.C. § 112, first paragraph, on the basis that "since the claimed invention is not supported by either a credible, specific, and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." Examiner's Answer, page 5. This rejection is simply a corollary of the finding of lack of utility.

Appellants argue that "[t]his rejection has been overcome by the arguments stated above regarding utility." Appeal Brief, page 14. We do not agree that Appellants' arguments overcome the rejection for lack of utility. Thus, our conclusion with respect to the § 101 issue also applies to the nonenablement rejection. On this basis we affirm the rejection of claim 1 under the enablement provision of 35 U.S.C. § 112, first paragraph.

4. Written description

The examiner rejected claims 1 and 2 under 35 U.S.C. § 112, first paragraph, for lack of adequate written description, reasoning that

[c]laim 1 is directed to a nucleic acid molecule "that encodes a plant protein or fragment thereof comprising." The specification fails to describe any open reading frames, start/stop codons, or encoded proteins for any SEQ ID NO. As such, these nucleic acid molecules are not described. At best, the SEQ ID NOS. may include a sequence encoding a fragment but not a full length protein.

The use of the term "comprising" is interpreted to encompass full length proteins and gene sequences that have not been disclosed. The common structural features of these encoded plant proteins or fragments are not disclosed and thus the claimed subject matter cannot be considered as being described.

The specification describes only the particular SEQ ID NOS. and no longer sequences containing them. One can only envision the particular sequence disclosed and cannot envision any encoded protein sequence or larger sequences in which the claimed SEQ ID NOS. are embedded.

Examiner's Answer, pages 5-6.

As we understand it, the examiner's rejection has two bases. First, the claimed nucleic acids are not adequately described because the preamble of claim 1 states that the each of the nucleic acids "encodes a plant protein or fragment thereof," and the specification does not describe any encoded proteins.

We will not sustain the rejection on this basis. The claims are directed to nucleic acids, not proteins, and the specification describes the complete sequence of each of the SEQ ID NOs that define the scope of the claimed nucleic acids. In addition, as we have construed the claims, the phrase that the examiner objects to ("encodes a plant protein or fragment thereof") has no patentable weight because it merely recites an inherent property that is expected for the claimed nucleic acids, based on the method by which they were isolated.

The second basis of the rejection, as we understand it, is that because of the transitional phrase "comprising", the claims encompass a large genus of nucleic acid molecules which are not adequately described by the SEQ ID NOs recited in the claim. See the Examiner's Answer, pages 18-20. Apparently, the examiner is of the opinion that the claimed invention should be limited to the nucleic acid molecules set forth in the recited SEQ ID NOs.

In response, Appellants argue that "[t]he fact that the claims at issue are intended to cover molecules that include the recited sequences joined with additional sequences does not mean that Applicants were any less in possession of the claimed nucleic acid molecules." Appeal Brief, page 16.

We have interpreted the claims to allow for the addition of nucleotides or other molecules at either end of the nucleotide sequences set forth in the recited SEQ ID NOs, but not to allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequences of the recited SEQ ID NOs. See pages 4-5, supra. We agree with Appellants that the claims, so interpreted, are supported by an adequate written description in the specification. The fact that the claimed nucleic acid molecules may

have other molecules attached to either or both of their 5' or 3' ends does not diminish Appellants' adequate written description of the nucleic acids molecules with the sequences set forth in the recited SEQ ID NOs, as claimed.

Accordingly, we reverse the rejection of claims 1 and 2 for lack of adequate written description.

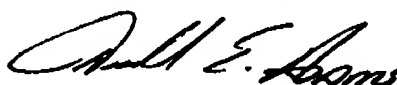
Summary

Although we reverse the examiner's rejection for lack of adequate written description, we affirm the rejection of claims 1 and 2 for lack of patentable utility.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED


WILLIAM F. SMITH
Administrative Patent Judge


DONALD E. ADAMS
Administrative Patent Judge


ERIC GRIMES
Administrative Patent Judge

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) BOARD OF PATENT
) APPEALS AND
) INTERFERENCES
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Appeal No. 2003-1:
Application No. 09/540,232

Page 27

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The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 25

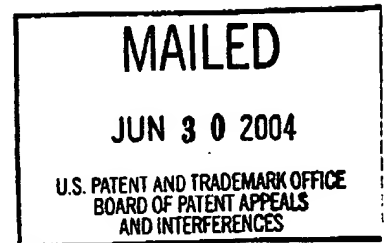
UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte JOSEPH R. BYRUM,
GREGORY R. HECK, and THOMAS J. LA ROSA

Appeal No. 2003-1504
Application No. 09/440,687

ON BRIEF¹



Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

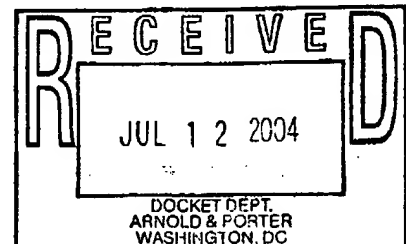
ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1 and 8-19. Claim 1 is illustrative of the subject matter on appeal and is reproduced below.

1. A substantially purified nucleic acid molecule that encodes a soybean protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 10.

The examiner does not rely on a reference.



¹ Appellants waived their request for oral hearing. Paper No. 24. Accordingly, we considered this appeal on Brief.

GROUND OF REJECTION

Claims 1 and 8-19 stand rejected under 35 U.S.C. § 101 as lacking utility and § 112, first paragraph, for lack of enablement based on the finding of lack of utility.

Claims 1 and 8-18 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification that fails to adequately describe the claimed invention.

We affirm the utility rejections under 35 U.S.C. § 101 and § 112, first paragraph and reverse the written description rejection under 35 U.S.C. § 112, first paragraph.

BACKGROUND

The subject matter of the present appeal is directed to expressed sequence tags. "Expressed sequence tags, or ESTs, are short sequences of randomly selected clones from a cDNA (or complementary DNA) library which are representative of the cDNA inserts of these randomly selected clones." Specification, page 1.

According to appellants (id.), "[t]he invention relates to nucleic acid molecules that encode proteins and fragments of proteins produced in plant cells, in particular, soybean plants." More particularly, appellants disclose "[t]he present invention provides a substantially purified nucleic acid molecule that encodes a soybean protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 31[,],015." Specification, page 9.

Of the 31,015 sequences disclosed in appellants' specification, the original claims filed with the application were directed to nucleic acid molecules that comprise a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1 – 4,486. On May 25, 2000 (Paper No. 4), the examiner entered a Restriction requirement into the record, requiring, inter alia, appellants to elect up to 10 independent and distinct nucleotide sequences. Paper No. 4, bridging paragraph, pages 2-3. In response, appellants elected SEQ ID NOs: 1-10². Paper No. 5, page 2.

CLAIM CONSTRUCTION

As set forth above, claim 1 on appeal is drawn to a substantially purified nucleic acid molecule that encodes a soybean protein or fragment thereof comprising nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 10. According to appellants' specification (bridging paragraph, pages 16-17), the term "substantially purified" refers

to a molecule separated from substantially all other molecules normally associated with it in its native state. More preferably a substantially purified molecule is the predominant species present in a preparation. A substantially purified molecule may be greater than 60% free, preferably 75% free, more preferably 90% free, and most preferably 95% free from the other molecules (exclusive of solvent) present in the natural mixture. The term "substantially purified" is not intended to encompass molecules present in their native state.

² Appellants disclose (specification, page 87), SEQ ID NO: 1 through SEQ ID NO: 4486 were obtained from the cDNA library LIB3040 which was "generated from soybean cultivar Asgrow 3244...."

As we understand the subject matter of claim 1, the transitional term "comprising" does not allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequences set forth in SEQ ID NOs: 1-10, but instead only allows for the addition of nucleotides or other molecules³ at either end of the nucleotide sequences.

In this regard, we recognize, as does the examiner (Answer, page 7), "[t]he claims encompass the nucleic acid for the gene (including introns and other non-coding information)...." For example, as explained by appellants (Brief, page 14),

[t]he present application describes more than just the nucleotide sequence required by the claims (SEQ ID NOs: 1 through 10), for example, it describes vectors comprising the claimed nucleic acid molecules ... [and] the addition of extra nucleotides or detectable labels to the disclosed nucleotide sequences.

The preamble of claim 1 also recites that the claimed nucleic acid molecule "encodes a soybean protein or fragment thereof." This phrase, however, merely recites an inherent function expected for the nucleic acid molecule defined by the SEQ ID NOs set forth in the claim; since the recited sequences were isolated as ESTs from soybean tissue, they would be expected to encode (parts of) soybean proteins. Since the introductory phrase does not further limit the invention defined by the body of the claim, it is irrelevant to construction of the claim. See IMS Technology, Inc. v. Haas Automation, Inc., 206 F.3d 1422, 1434, 54 USPQ2d 1129, 1137 (Fed. Cir. 2000) ("If the preamble

³ According to appellants' specification (page 17), "agents of the present invention may be labeled with reagents that facilitate detection of the agent (e.g., fluorescent labels, ... chemical labels, ... [and] modified bases...."

adds no limitations to those in the body of the claim, the preamble is not itself a claim limitation and is irrelevant to proper construction of the claim.").

Accordingly, for the purposes of our review, we interpret the claimed invention as drawn to a nucleic acid molecule, separated from substantially all other molecules normally associated with it in its native state, that comprises a nucleotide sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 10, with or without any preceding or trailing nucleotides, or other molecules.

DISCUSSION

Utility

The starting point for determining whether the nucleic acid molecule of claim 1⁴ possesses utility under 35 U.S.C. § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). As set forth in Brenner, at 534-35, 148 USPQ at 695⁵,

the basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until [an invention] is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

⁴ According to appellants (Brief, page 3), "[p]atentability of claims 1 and 8-19 is addressed together..." We interpret this statement to mean that claims 1 and 8-19 stand or fall together. Accordingly, we limit our discussion to representative independent claim 1. Claims 8-19 will stand or fall together with claim 1. In re Young, 927 F.2d 588, 590, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991).

⁵ In discussing the issue of utility under 35 U.S.C. § 101, the Federal Circuit and the Court of Customs and Patent Appeals since Brenner, have used the phrases "substantial utility" and "practical utility" interchangeably. See e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1563-64, 39 USPQ2d 1895, 1898-1899 (Fed. Cir. 1996) ("It is well established that a patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed.").

In considering the issues presented in this appeal, special attention must be paid to the Brenner court's statement that a patent should issue only when an invention possesses "substantial utility," i.e., "where a specific benefit exists in currently available form." Whether a claimed invention is useful under 35 U.S.C. § 101 is a question of fact. Cross v. Iizuka, 753 F.2d 1040, 1044 n.7, 224 USPQ 739, 742 n.7 (Fed. Cir. 1985).

At issue in Brenner was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that "where a claimed process produces a known product it is not necessary to show utility for the product." Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be "useful," that "simple, everyday word can be pregnant with ambiguity when applied to the facts of life." Id. at 529, 148 USPQ at 693. Thus,

[i]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new and useful" phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of "utility"—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.⁶

The Court, finding “no specific assistance in the legislative materials underlying § 101,” based its analysis on “the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other.” Id. at 532, 148 USPQ at 695. The Court concluded that “[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.” Id. at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant’s argument that attenuating the requirement of utility “would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge.” The Court noted that, while there is value to encouraging disclosure, “a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast,

⁶ The invention at issue in Brenner was a process, but the Court expressly noted that its holding “would apply equally to the patenting of the product produced by the process.” Id. at 535, 148

unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroidal research and in the application of steroidal materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help

their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" Id. at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a

rejection based on an intervening reference. Id. “[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there.” Id.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were “well recognized in the art as valuable for use in cancer chemotherapy.” Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were “relevant to the treatment of humans and [were] not to be disregarded,” id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that “[it] is axiomatic that an invention cannot be considered ‘useful,’ in the sense that a patent can be granted on it, unless substantial or practical utility for the invention

has been discovered and disclosed where such utility would not be obvious." Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court "perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question." Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by "marshal[ling] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds ..., analogous to the benefit provided by the showing of an in vivo utility." Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk,

376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best ... on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, at 1203, 26 USPQ2d at 1605.

On this record, appellants assert (Brief, bridging paragraph, pages 5-6, footnotes omitted) that the specification sets forth a number of utilities for the claimed nucleic acid molecule

e.g., to detect the presence and/or identity of polymorphisms, and as hybridization probes for expression profiling ... [in addition to introducing] the claimed nucleic acid molecules into a plant or plant cell (as antisense inhibitors), which can then be used to screen for compounds such as a herbicide ... to measure the level of mRNA in a sample, and use as molecular markers.

We note, however, that the specification does not specifically disclose how to use a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 10, as set forth in claim 1. To the contrary, the specification describes the aforementioned utilities as applicable to all of the nucleic acid molecules set forth in SEQ ID NO: 1 through SEQ ID NO: 31,015. See e.g., specification, pages 9-15. We note, however, that appellants discuss the potential activity of populations of nucleic acid molecules that includes less than all 31,015 nucleic acid sequences. See specification, pages 32-35. This section describes the cDNA libraries from which specific populations of nucleotide sequences were obtained. As discussed supra, SEQ ID NO: 1 through SEQ ID NO: 4,486 were obtained from the cDNA

library LIB3040. Specification, page 87. According to appellants' specification (bridging paragraph, pages 32-33),

[t]he ESTs of ... [the LIB3040] library can enable acquisition of, but are not limited to, genes involved in seed development, therefore, the ESTs of the present invention will also find great use in the isolation of a variety of agronomically significant genes, including but not limited to genes that regulate proteins, amino acids, sterols, oils, minerals, isoflavones, saponins, trypsin inhibitors, vitamins, tocopherols, antinutrient components, carbohydrates, starch metabolism, and seed regulatory elements. Such genes are associated with plant growth, quality, yield, and could also serve as links in important metabolic, developmental and catabolic pathways.

Appellants, however, fail to disclose which of the aforementioned activities, if any, can be attributed to a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 10.

Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal, i.e., identification and detection of polymorphisms and use as probes or as a source for primers. We shall focus on these asserted utilities first and then address the other arguments set forth in the briefing.

a. Polymorphisms

This utility is discussed at pages 40-47 of the specification in terms of what polymorphisms are and how one would go about determining the existence of a polymorphism. The discussion in this portion of the specification, however, is not specific to the nucleotide molecule set forth in claim 1. To the contrary, according to appellants' specification (e.g., page 46, lines 15-16), "one or more of the [31,015] nucleic acids of the present invention, may be utilized as markers or probes to detect polymorphisms...."

The specification does not explain why any of the 31,015 nucleic acid molecules disclosed in the specification, or more specifically a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 10 would in fact be useful in detecting polymorphisms. Rather, appellants argue (Brief, page 7), "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." In other words, appellants' position is that a nucleic acid by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. See e.g., Brief, page 10. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by a nucleic acid, as here, detection of the presence or absence of a

polymorphism provides the barest information in regard to genetic heritage. As the examiner explains (Answer, page 12), appellants' specification defines "polymorphism" as

"a variation or difference in the sequence of the gene or its flanking regions that arises in some members of a species." It follows from this definition that if there is no "variation or difference in the sequence of the gene or its flanking regions" among "members of a species," then no polymorphism exists, i.e. a polymorphism is absent, in this region of the genome.

According to the examiner (Answer, page 11), "the presence or absence of any of the claimed nucleotide sequences in a sample (or polymorphisms thereof) has no meaning absent some association. Further experimentation is required to determine what, if any, that meaning or association might be." In this regard, the examiner finds (Answer, page 12), appellants' specification "does not disclose whether the claimed nucleic acid molecules can, in fact, be used to detect any polymorphism whatsoever. Thus, the specification leaves open the possibility that there may be no polymorphism to detect." According to the examiner (Answer, bridging paragraph, pages 12-13), "[t]he specification generally teaches using a polymorphism, detectable with the claimed nucleic acid molecules, as a molecular marker for a linked trait of interest, but fails to teach either the polymorphism or the trait of interest." According to the examiner (Answer, page 14), "the specification fails to identify even one specific polymorphism that can be detected with the claimed nucleic acid molecule, the specification fails to show any specific correspondence between the disclosed general utility and the claimed subject matter, regardless of any specific application requiring detection of polymorphisms." Accordingly the examiner finds (id.), "using the claimed

invention to first determine whether or not the claimed nucleic acid molecule can, in fact, detect a polymorphism is to determine whether or not the claimed invention has a utility that requires detecting a polymorphism, i.e. it is 'use testing' and not substantial."

In contrast, at the other end of the "utility spectrum" would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene from which the nucleic acid is derived has in the development and/or phenotype of the plant. Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the gene and its role in the plant's development and/or phenotype lies the line between "utility" and "substantial utility." We need not draw the line or further define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.⁷

b. Probes or source of primers

Appellants assert that the "specification discloses that the claimed nucleic acid molecules can be used ... to isolate nucleic acid molecules of other plants and organisms...." Brief, page 8. While that may be true, it begs the question of what substantial use such nucleic acid molecules would have? Again, the present specification does not attribute any property in terms of plant trait, or

⁷ For the foregoing reasons, we disagree with appellants' assertion (Brief, page 3) that the claimed nucleic acid molecule provides "at least one specific benefit to the public, for example the ability to identify the presence or absence of a polymorphism."

phenotype to the nucleic acid molecule set forth in claim 1. In the absence of such information, using the claimed molecule to isolate other molecules, which themselves lack substantial utility, does not represent a substantial utility.⁸

Appellants also assert that the claimed nucleic acid molecule may be used in a "chromosome walk." Brief, page 8. According to appellants (Brief, page 9),

The claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter that is active in soybean. ... A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter. Furthermore, even if a random nucleic acid molecule provided a better starting point than the claimed nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules.

As we understand this argument, the claimed nucleic acid may be useful in searching for promoters that are active in soybeans. The specification, however, fails to demonstrate that a nucleic acid molecule as set forth in claim 1 would be useful in obtaining a successful result from such a search. As set forth at page 38, lines 15-20 of appellants' specification,

The [31,015] nucleic acid molecules of the present invention may be used to isolate promoters of tissue enhanced, tissue specific, cell-specific, cell -type, developmentally or environmentally regulated expression profiles. Isolation and functional analysis of the 5' flanking promoter sequences of these genes from genomic libraries, for example, using genomic screening methods and PCR techniques would result in the isolation of useful promoters and transcriptional regulatory elements.

⁸ In addition, we note the examiner's assertion (Answer, page 16), "[a]t the time the application had been filed, future experimentation on the part of one skilled in the art would have been required to determine which, if any, other plant species contained nucleic acid molecules that could have been obtained using the claimed invention, and under what experimental conditions."

The specification does not provide any expectation of successfully using any of the 31,015 nucleic acid molecules disclosed in the specification, or more specifically the nucleic acid molecule of claim 1 to isolate promoters of tissue enhanced, tissue specific, cell-specific, cell-type, developmentally or environmentally regulated expression profiles. According to the examiner (Answer, page 16), "the specification fails to disclose any characteristics of the corresponding promoter, or any other promoter within 'chromosome walking' distance; neither structural characteristics, by which the promoter might be identified, nor functional characteristics, by which a specific and substantial use for the promoter might be determined." By way of example, the examiner argues (Answer, page 17), assume

a nucleotide sequence is identified during the chromosome walk as a putative promoter by sequence analysis, is then subcloned into operable linkage with a reporter gene and transfected into an appropriate cell, but found not to express the reporter gene in the cells. This result could mean the putative promoter: is not truly a promoter, i.e. a false positive; is not the corresponding promoter; or is incomplete, i.e. lacked additional sequence elements required for promoter activity in the seed pod cells.

According to the examiner (Answer, page 11), appellants merely isolated the claimed nucleic acid molecule, "[t]hey have not tested, evaluated, or calibrated the claimed nucleotide sequence for any particular use."

We recognize appellants' argument (Brief, page 9), "[a]n invention may be 'less effective than existing devices but nevertheless meet the statutory criteria for patentability.' Custom Accessories, Inc. v. Jeffrey-Allan Indus., 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986)." While we agree with appellants' statement, we fail to see how it applies to appellants' claimed

invention, wherein there is no evidence or expectation that the claimed nucleic acid molecules would be "effective" at all. In this regard, we remind appellants that an invention does not have utility sufficient to satisfy § 101 until it is "refined and developed" to the point of providing a specific benefit in currently available form. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695.

An invention certainly can have a utility that is shared by other compounds or compositions. Take, for example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful as analgesics. On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

c. Other Arguments

Appellants argue that the specification "discloses additional utilities for the claimed nucleic acid molecules including introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for compounds such as a herbicide." Brief,

page 5. Specifically, appellants argue (id.) that "a compound can be provided to both an antisense plant and a control plant (no antisense) and the effect of the compound on the plant can be monitored." Appellants analogize this proposed procedure to a "cell-based assay" which appellants assert to have a "legally sufficient utility." Id.

However, the examiner finds (Answer, page 9), further research is required to use the claimed nucleic acid molecules "to detect the presence and/or identity of polymorphisms, as hybridization probes for expression profiling, as antisense inhibitors by introduction of the claimed nucleic acid molecule into a plant or plant cell where the resulting cell or plant is to be used to screen compounds such as herbicides, to measure the level of mRNA in a sample, and as a molecular marker." In addition, the examiner finds (id.), that since targets are not disclosed in the specification, the use of the claimed nucleic acid molecule "as antisense inhibitors would require further experimentation to determine the target of inhibition." To the extent that appellants would argue that the claimed nucleic acid could be used in assays that measure the presence of a material that correlates to a predisposed disease condition, the examiner finds (Answer, page 7), "[t]he instant specification sets forth no such correlation for any condition."

As to the use of the claimed nucleic acid in microarrays (see e.g., Brief, page 6, n. 4), the examiner finds (Answer, page 10), "[a]ppellant is [sic] not claiming microarrays or collections of nucleotides and the specification does not

associate the claimed sequence with any trait of interest." According to the examiner (Answer, page 10),

[c]ontrary to appellant's [sic] assertions, further experimentation is required to identify a "real world use." A negative result to such a screen tells what the nucleic acid is not and cannot be used for. A positive result to such a screen requires further experimentation to determine what, if anything, such a change means. It is not an immediate benefit except in the sense to indicate that further research might yield a "real world use."

Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. In regard to microarrays, we find that the asserted utility of the claimed nucleic acid—as one component of an assay for monitoring gene expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form. We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid molecule set forth in claim 1. However, the specification provides no guidance that would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification simply provides no guidance regarding what the specific information derived from a gene expression experiment would mean in the context of a nucleic acid molecule as set forth in claim 1.

To highlight the examiner's assertion (Answer, page 10), suppose, for example, that a researcher found that expression of the nucleic acid molecule set forth in claim 1 was increased when a cell was treated with a particular agent.

The specification provides no basis on which a skilled worker would be able to

determine whether that result is meaningful. Maybe the meaning in a change in expression would depend on other factors, but again the specification provides no hint as to what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), the degree of increase? The specification simply provides no guidance as to how to interpret the results that might be seen using the nucleic acid molecule of claim 1 in a gene expression assay.

In effect, appellants' position is that the claimed nucleic acids are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the present case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, because even if used in gene expression assays, the specification does not disclose how to use the specific gene expression data in the context of the nucleic acid molecule of claim 1.

Assuming arguendo, that a generic gene expression assay - one based on monitoring expression of thousands of uncharacterized nucleic acids - would provide a useful tool for, e.g., drug discovery, it does not follow that each one of the nucleic acids represented in the assay individually has patentable utility. Although each nucleic acid in the assay contributes to the data generated by the assay overall, the contribution of a single nucleic acid - its data point - is only a tiny contribution to the overall picture. The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently available form. Providing a single data point among thousands or millions, even if the thousands or millions of data points collectively are useful, does not meet this standard. The Supreme Court noted that the patent system contemplates a basic quid pro quo: in exchange for the legal right to exclude others from his invention for a period of time, an inventor discloses his invention to the public. See Brenner, 383 U.S. at 534, 148 USPQ at 695. The Brenner Court held that the grant of patent rights to an applicant is justified only by disclosure of an invention with substantial utility - a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the

applicant has not met his side of the bargain, and has not provided a disclosure sufficient to justify a grant of the right to exclude others. See id.

We reach the same conclusion in regard to appellants' assertion that the nucleic acid molecule set forth in claim 1 is useful as a molecular marker or probe. It is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of claim 1 as a molecular marker or probe represents a substantial use.

Appellants argue that ESTs have real world value as seen from the "growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs." Brief, page 10. Since appellants fail to provide any suggestion on which use of ESTs this industry is premised on, we can only assume that appellants are referring to the potential usefulness of EST databases, clone sets or microarrays. Suffice it to say, the claims on appeal are not directed to EST databases, clone sets and/or microarrays. Again, it is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of claim 1 in such devices represents a substantial use.

Further, we understand appellants' position to be that a compound would be patentable if it was adequately described in the specification and was not disclosed or suggested in the prior art. This standard, however, is not the one set by Congress, which requires that a patentable invention also be useful and fully enabled, nor is it the standard that has been consistently applied by the courts.

Not only is appellants' proposed utility standard contrary to controlling case law, but there are reasons to expect that it would hurt – rather than help – the microarray industry. Under appellants' standard, any naturally occurring gene, and fragments thereof, would be held to have patentable utility based on its use in generating expression data. The practical effect of this standard would be that making a microarray with, e.g., 1000 genes represented on it would require investigating the patent status of each oligonucleotide on the microarray. Not only that, but since appellants assert that their reasoning supports the utility of gene fragments, all of the subsequences of each of the genes would have to be checked to ensure that they were not the subject of someone else's patent.

For each of the genes (or fragments thereof) that was the subject of a patent claim held by someone else, a license would have to be negotiated – potentially thousands of such negotiations for the finished product. These transaction costs would have to be incurred for each new product that an aspiring microarray manufacturer wished to market. The industry gridlock likely to result from this scenario has been termed a "tragedy of the anticommons".⁹

By conferring monopolies in discoveries, patents necessarily increase prices and restrict use—a cost society pays to motivate invention and disclosure. The tragedy of the anticommons refers to the more complex obstacles that arise when a user needs access to multiple patented inputs to create a single useful product. Each upstream patent allows its owner to set up another tollbooth on the

⁹ Heller et al., "Can patents deter innovation? The anticommons in biomedical research," *Science*, Vol. 280, pp. 698-701 (1998). Available online at www.sciencemag.org/cgi/content/full/280/5364/698.

road to product development, adding to the cost and slowing the pace of downstream biomedical innovation.

Heller, page 698.

The Supreme Court has warned against allowing too many tollbooths on the road to innovation:

Patents . . . are meant to encourage invention by rewarding the inventor with the right, limited to a term of years fixed by the patent, to exclude others from the use of his invention. . . . But in rewarding useful invention, the "rights and welfare of the community must be fairly dealt with and effectually guarded." Kendall v. Winsor, 21 How. 322, 329 (1859).... To begin with, a genuine "invention" or "discovery" must be demonstrated "lest in the constant demand for new appliances the heavy hand of tribute be laid on each slight technological advance in an art."

Sears, Roebuck & Co. v. Stiffel Co., 376 U.S. 225, 230, 140 USPQ 524, 527 (1964).

We note that the examiner acknowledges appellants' assertion (Brief, page 5, n. 2), "[i]t is irrelevant whether the corresponding mRNA or polypeptide have utility because [a]pplicants are not relying on utility of the mRNA or polypeptide to establish utility of the claimed nucleic acid molecules." Answer, page 8. Nevertheless, the examiner asserts (Answer, bridging sentence, pages 8-9), "[t]he [B]rief does not dispute that no open reading frame (ORF), no encoded protein, nor any biological activity for any encoded protein has been disclosed for SEQ ID NOS: 1-10."

As for non-asserted utilities, the examiner finds (Answer, page 6), "there is no evidence of a well-established utility for the disclosed ESTs or claimed nucleic acid molecules."

The basic guid pro quo of the patent system requires disclosure of an invention having substantial utility. On reflection, we find appellants' disclosure in this case does not provide a specific benefit in currently available form, and therefore lacks the substantial utility required by 35 U.S.C. § 101. For the foregoing reasons we affirm the rejection of claim 1 under 35 U.S.C. § 101. As discussed supra, claims 8-19 fall together with claim 1.

Enablement

According to the examiner (Answer, page 6), "since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." This rejection is simply a corollary of the finding of lack of utility. Appellants assert (Brief, page 12), "[t]his rejection was erroneous and has been overcome by the arguments stated above regarding ... [the rejection under 35 U.S.C. § 101]." Thus, our conclusion with respect to the § 101 issue will also apply to this aspect of the § 112 (enablement) issue. On this basis we affirm the rejection of claim 1 under the enablement provision of 35 U.S.C. § 112, first paragraph. As discussed supra, claims 8-19 fall together with claim 1.

Written description

The examiner rejected claims 1 and 8-18 under 35 U.S.C. § 112, first paragraph, for lack of an adequate written description. According to the examiner (Answer, page 7),

[t]he claims encompass the nucleic acid for the gene (including introns and other non-coding information) within the scope of the invention by virtue of the "comprising" and "encoding" language." ... Neither the structural and functional properties of any gene comprising SEQ ID NOS: 1-10 nor the structural and functional properties of any protein or fragment thereof encoded by a nucleotide sequence comprising SEQ ID NOS: 1-10 are disclosed in the specification.

As we understand it, the examiner's rejection has two bases. First, the claimed nucleic acids are not adequately described because the preamble of claim 1 states that the claimed nucleic acid molecule "encodes a soybean protein or fragment thereof," and the specification does not describe any encoded proteins.

We will not sustain the rejection on this basis. The claims are directed to nucleic acid molecules, not proteins, and the specification describes the complete sequence of each of the SEQ ID NOs that define the scope of the claimed nucleic acid molecules. In addition, as we have construed the claims, the phrase that the examiner objects to ("encodes a soybean protein or fragment thereof") has no patentable weight because it merely recites an inherent property that is expected for the claimed nucleic acids, based on the method by which they were isolated.

The second basis of the rejection, as we understand it, is that because of the transitional phrase "comprising", the claims encompass a large genus of

nucleic acid molecules, which are not adequately described by the SEQ ID NOs recited in the claim. See Answer, pages 19-22. Apparently, the examiner is of the opinion that the claimed invention should be limited to the nucleic acid molecules set forth in the recited SEQ ID NOs.

We have interpreted the claims to allow for the addition of nucleotides or other molecules at either end of the nucleotide sequences set forth in the recited SEQ ID NOs, but not to allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequences of the recited SEQ ID NOs. See pages 3-5, supra. The fact that the claimed nucleic acid molecules may have other molecules attached to either or both of their 5' or 3' ends does not diminish Appellants' adequate written description of the nucleic acids molecules with the sequences set forth in the recited SEQ ID NOs, as claimed.

Accordingly, we reverse the rejection of claims 1 and 8-18 for lack of adequate written description.

Summary


We affirm the utility rejections under 35 U.S.C. § 101 and § 112, first paragraph.

We reverse the written description rejection under 35 U.S.C. § 112, first paragraph.

No time period for taking any subsequent action in connection with this
appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED


William F. Smith
Administrative Patent Judge


Donald E. Adams
Administrative Patent Judge


Eric Grimes
Administrative Patent Judge

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The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 25

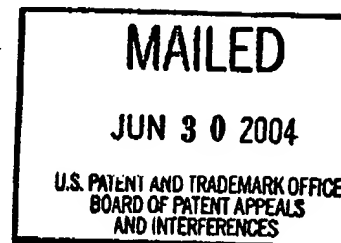
UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte MARK S. ABAD and THOMAS J. LA ROSA

Appeal No. 2003-1135
Application No. 09/565,240

ON BRIEF¹



Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

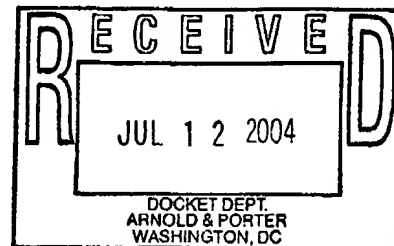
ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claim 1, which is reproduced below.

1. A substantially purified nucleic acid molecule that encodes a soybean protein or soybean protein fragment comprising the nucleic acid sequence of SEQ ID NO: 49441.

The examiner does not rely on a reference.



¹ Appellants waived their request for oral hearing. Paper No. 24. Accordingly, we considered this appeal on Brief.

GROUND OF REJECTION

Claim 1 stands rejected under 35 U.S.C. § 101 as lacking utility and § 112, first paragraph, for lack of enablement based on the finding of lack of utility. We affirm.

BACKGROUND

According to appellants' specification (page 1), "[t]he invention relates to nucleic acid molecules that encode proteins and fragments of proteins produced in plant cells, in particular, soybean plants." More particularly, appellants disclose "[t]he present invention provides a substantially purified nucleic acid molecule that encodes a soybean protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 54[,]005." Specification, page 9.

Of the 54,005 sequences disclosed in appellants' specification, the original claims filed with the application were directed to nucleic acid molecules that comprise a nucleic acid sequence selected from the group consisting of SEQ ID Nos: 49,441 – 54,005. On February 9, 2001 (Paper No. 2), the examiner entered a Restriction requirement into the record, requiring, inter alia, appellants to elect a single nucleic acid sequence for consideration on the merits. Paper No. 2, page 2. In response, appellants elected SEQ ID NO: 49,441². Paper No. 5, page 2.

² Appellants disclose (specification, page 98, as amended in Paper No. 11, pages 8-9), SEQ ID NO: 49,441 was obtained from the cDNA library LIB3167.

CLAIM CONSTRUCTION

As set forth above, claim 1 on appeal is drawn to a substantially purified nucleic acid molecule that encodes a soybean protein or soybean protein fragment comprising the nucleic acid sequence set forth in SEQ ID NO: 49,441.

According to appellants' specification (page 17), the term "substantially purified"

refers to a molecule separated from substantially all other molecules normally associated with it in its native state. More preferably a substantially purified molecule is the predominant species present in a preparation. A substantially purified molecule may be greater than 60% free, preferably 75% free, more preferably 90% free, and most preferably 95% free from the other molecules (exclusive of solvent) present in the natural mixture. The term "substantially purified" is not intended to encompass molecules present in their native state.

As we understand the subject matter of claim 1 the transitional term "comprising" does not allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequences set forth in SEQ ID NO: 49,441, but instead only allows for the addition of nucleotides or other molecules³ at either end of the nucleotide sequence set forth in SEQ ID NO: 49,441. In this regard, we recognize, as does the examiner (Answer, page 4), the claim as written encompasses, inter alia, any full length gene, fusion construct, RNA or cDNA that comprises the nucleotide sequence set forth in SEQ ID NO: 49,441 and is capable of encoding at least a fragment of a soybean protein.

³ According to appellants' specification (page 17), "agents of the present invention may be labeled with reagents that facilitate detection of the agent (e.g., fluorescent labels, ... chemical labels, ... [and] modified bases...."

Accordingly, for the purposes of our review, we interpret the claimed invention as drawn to a nucleic acid molecule, separated from substantially all other molecules normally associated with it in its native state, that comprises the nucleotide sequence set forth in SEQ ID NO: 49,441 with or without any preceding or trailing nucleotides, or other molecules.

DISCUSSION

Utility

The starting point for determining whether the nucleic acid molecule of claim 1 possesses utility under 35 U.S.C. § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). As set forth in Brenner, at 534-35, 148 USPQ at 695⁴,

the basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until [an invention] is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

In considering the issues presented in this appeal, special attention must be paid to the Brenner court's statement that a patent should issue only when an invention possesses "substantial utility," i.e., "where a specific benefit exists in currently available form." Whether a claimed invention is useful under 35 U.S.C.

⁴ In discussing the issue of utility under 35 U.S.C. § 101, the Federal Circuit and the Court of Customs and Patent Appeals since Brenner, have used the phrases "substantial utility" and "practical utility" interchangeably. See e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1563-64, 39 USPQ2d 1895, 1898-1899 (Fed. Cir. 1996) ("It is well established that a patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed.").

§ 101 is a question of fact. Cross v. Iizuka, 753 F.2d 1040, 1044 n.7, 224 USPQ 739, 742 n.7 (Fed. Cir. 1985).

At issue in Brenner was a claim to “a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced.” Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that “where a claimed process produces a known product it is not necessary to show utility for the product.” Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be “useful,” that “simple, everyday word can be pregnant with ambiguity when applied to the facts of life.” Id. at 529, 148 USPQ at 693. Thus,

[i]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the “new and useful” phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man’s grasp and where little or nothing is wholly beyond the pale of “utility”—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.⁵

⁵ The invention at issue in Brenner was a process, but the Court expressly noted that its holding “would apply equally to the patenting of the product produced by the process.” Id. at 535, 148 USPQ at 695-96.

The Court, finding “no specific assistance in the legislative materials underlying § 101,” based its analysis on “the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other.” Id. at 532, 148 USPQ at 695. The Court concluded that “[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.” Id. at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant’s argument that attenuating the requirement of utility “would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge.” The Court noted that, while there is value to encouraging disclosure, “a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development.” Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not “mean to disparage the importance of contributions to the fund of scientific information short of the invention of something ‘useful,’” and that it was not “blind to the prospect that what now seems without ‘use’ may tomorrow command the grateful attention of the public.” Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because “a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.” Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101’s utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value “in the furtherance of steroidal research and in the application of steroidal materials to veterinary or medical practice.” Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly “show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests.” Id. at 939, 153 USPQ at 51.

The court held that “nebulous expressions [like] ‘biological activity’ or ‘biological properties’” did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants’ affidavit help their case: “the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know ‘how to use’ the compounds to find out in the

first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" Id. at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. Id. "[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of

the German application; but in that application Ziegler had not yet gotten there.”

Id.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were “well recognized in the art as valuable for use in cancer chemotherapy.” Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were “relevant to the treatment of humans and [were] not to be disregarded,” id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that “[it] is axiomatic that an invention cannot be considered ‘useful,’ in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious.” Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court “perceive[d] no

insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question.” Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by “marshal[ling] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds ..., analogous to the benefit provided by the showing of an in vivo utility.” Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk,

376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best ... on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, at 1203, 26 USPQ2d at 1605.

On this record, appellants assert (Brief, bridging paragraph, pages 5-6) that specification sets forth a number of utilities for the

present invention, including "probes for assisting in the isolation of full-length cDNAs or genes which would be used to make protein and optionally further usage to make the corresponding antibodies, gene mapping, isolation of homologous sequences, detection of gene expression such as in Northern blot analysis, molecular weight markers, chromosomal markers, and for numerous other generic genetic engineering usages." ... In addition to ... detecting the presence and level of mRNA in a sample; identifying polymorphisms; obtaining promoters and other flanking genetic elements to such molecules; determining the location of a corresponding DNA sequence on a genetic map; isolating related nucleic acid and protein molecules; and conducting plant transformation or transfection; etc....

We note, however, that the specification does not specifically disclose how to use a nucleic acid molecule comprising the nucleic acid sequence set forth in SEQ ID NO: 49,441, as set forth in claim 1. To the contrary, the specification describes the aforementioned utilities as applicable to all of the nucleic acid molecules set forth in SEQ ID NO: 1 through SEQ ID NO: 54,005. See e.g., specification, pages 9-15. We note, however, that appellants discuss the potential activity of (specification, pages 33-39) populations of nucleic acid molecules that includes less than all 54,005 nucleic acid sequences. This section describes the cDNA libraries from which specific populations of

nucleotide sequences were obtained. As discussed supra, SEQ ID NO: 49,441 through SEQ ID NO: 54,005 were obtained from the cDNA library LIB3167.

Specification, page 98, as amended in Paper No. 11, pages 8-9. According to appellants' specification (bridging paragraph, pages 38-39),

the [LIB3167] cDNA library of the present invention can enable acquisition of, including but not limited to, stress response genes and genes that regulate PR proteins ... the ESTs of the present invention will also find great use in the isolation of a variety of agronomically significant genes, including but not limited to genes that regulate germination, developmental stress, protein, amino acids, sterols, oils, minerals, isoflavones, saponins, trypsin inhibitors, vitamins, tocopherols, antinutrient components, carbohydrates, starch metabolism, and seedling and vegetative regulatory elements. Such genes are associated with plant growth, quality, yield, and could also serve as links in important metabolic, developmental and catabolic pathways.

Appellants, however, fail to disclose which of the aforementioned activities, if any, can be attributed to the nucleic acid molecule comprising the sequence set forth in SEQ ID NO: 49,441, or a protein or protein fragment encoded thereby.

Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal, i.e., identification and detection of polymorphisms and use as probes or as a source for primers. We shall focus on these asserted utilities first and then address the other arguments set forth in the briefing.

a. Polymorphisms

This utility is discussed at pages 43-55 of the specification in terms of what polymorphisms are and how one would go about determining the existence of a polymorphism. The discussion in this portion of the specification, however,

is not specific to the nucleotide molecule set forth in claim 1. To the contrary, according to appellants' specification (e.g., page 50, lines 7-9), "one or more of the [54,005] nucleic acids of the present invention, may be utilized as markers or probes to detect polymorphisms...."

The specification does not explain why any of the 54,005 nucleic acid molecules disclosed in the specification, or more specifically a nucleic acid molecule comprising the nucleic acid sequence set forth in SEQ ID NO: 49,441 would in fact be useful in detecting polymorphisms. Rather, appellants argue (Brief, page 7), "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." In other words, appellants' position is that a nucleic acid by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. See e.g., Brief, page 10. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by the nucleic acid, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage. As the examiner explains (Answer, page 7),

While agreement is reached in that some polymorphisms have been found to be useful as a result of their presence having been correlated with another event, e.g., the development of cancer in an individual, the over or under expression of one or more genes that has in turn a specific effect that has known value. In the

present case, however, the claimed nucleic acid sequence has not been tightly associated with any one protein. Indeed, the appellant is less than [sic] assured that the claimed nucleic acid encodes an intact protein or a fragment of a soybean protein....

Stated differently, whether the claimed nucleotide sequence is capable of detecting the presence or absence of a polymorphism has no meaning absent some association.

In contrast, at the other end of the "utility spectrum" would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene from which the nucleic acid is derived has in the development and/or phenotype of the plant. Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the gene and its role in the plant's development and/or phenotype lies the line between "utility" and "substantial utility." We need not draw the line or further define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.⁶

b. Probes or source of primers

Appellants assert that the "specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms...." Brief, page 7. While that may be true, it begs the question of what substantial use such nucleic acid molecules would have? Again, the present specification does not attribute any property in terms of plant trait, or

⁶ For the foregoing reasons, we disagree with appellants' assertion (Brief, page 3) that the claimed nucleic acid molecule provides "at least one specific benefit to the public, e.g., the ability to identify the presence or absence of a polymorphism in a population of soybean plants."

phenotype to any of the nucleic acid molecule set forth in claim 1. In the absence of such information, using the claimed molecule to isolate other molecules, which themselves lack substantial utility, does not represent a substantial utility.

Appellants also assert that the claimed nucleic acid molecules may be used in a "chromosome walk" or to isolate "the promoter of the gene corresponding to the claimed nucleic acid molecules." Brief, page 8. As we understand this argument, the claimed nucleic acid may be useful in searching for promoters. The specification, however, fails to demonstrate that the nucleic acid molecule set forth in claim 1 would be useful in obtaining a successful result from such a search. As set forth in appellants' specification (bridging paragraph, pages 41-42),

The [54,005] nucleic acid molecules of the present invention may be used to isolate promoters of tissue enhanced, tissue specific, cell-specific, cell -type, developmentally or environmentally regulated expression profiles. Isolation and functional analysis of the 5' flanking promoter sequences of these genes from genomic libraries, for example, using genomic screening methods and PCR techniques would result in the isolation of useful promoters and transcriptional regulatory elements.

The specification, however, does not provide any expectation of successfully using any of the 54,005 nucleic acid molecules disclosed in the specification, or more specifically the nucleic acid molecule of claim 1 to isolate promoters having cell enhanced, cell specific, tissue enhanced, tissue specific, developmentally or environmentally regulated expression profiles.

We agree with appellants' assertion (Brief, page 8) that an invention certainly can have a utility that is shared by other compounds or compositions. Take, for example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful as analgesics. On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101. In this regard, we note the examiner's argument (Answer, page 8), "a review of the disclosure fails to find where any specific chromosome as being a target for initiating chromosome walking or for otherwise marking a specific region of interest of a given chromosome. Accordingly, the utility asserted is considered to be 'general' and not 'specific'."

c. Other Arguments

Appellants argue that ESTs have real world value as seen from the "growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs." Brief, page 11. Since appellants fail to provide any suggestion on which use of ESTs this industry is premised on, we can only

assume that appellants are referring to the potential usefulness of EST databases, clone sets or microarrays. Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. In regard to microarrays, we find that the use of the claimed nucleic acid—as one component of an assay for monitoring gene expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form. We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid molecule set forth in claim 1. However, the specification provides no guidance that would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification simply provides no guidance regarding what the specific information derived from a gene expression experiment would mean in the context of a nucleic acid molecule as set forth in claim 1.

Suppose, for example, that a researcher found that expression of the nucleic acid molecule set forth in claim 1 was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. Maybe the meaning in a change in expression would depend on other factors, but again the specification provides no hint as to what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), the degree of

increase? The specification simply provides no guidance as to how to interpret the results that might be seen using the nucleic acid molecule of claim 1 in a gene expression assay.

In effect, appellants' position is that the claimed nucleic acids are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the present case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, because even if used in gene expression assays, the specification does not disclose how to use the specific gene expression data in the context of the nucleic acid molecule of claim 1.

Assuming arguendo, that a generic gene expression assay - one based on monitoring expression of thousands of uncharacterized nucleic acids - would provide a useful tool for, e.g., drug discovery, it does not follow that each one of the nucleic acids represented in the assay individually has patentable utility. Although each nucleic acid in the assay contributes to the data generated by the

assay overall, the contribution of a single nucleic acid—its data point—is only a tiny contribution to the overall picture. The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently available form.

Providing a single data point among thousands or millions, even if the thousands or millions of data points collectively are useful, does not meet this standard.

The Supreme Court noted that the patent system contemplates a basic quid pro quo: in exchange for the legal right to exclude others from his invention for a period of time, an inventor discloses his invention to the public. See Brenner, 383 U.S. at 534, 148 USPQ at 695. The Brenner Court held that the grant of patent rights to an applicant is justified only by disclosure of an invention with substantial utility – a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the applicant has not met his side of the bargain, and has not provided a disclosure sufficient to justify a grant of the right to exclude others. See id.

We reach the same conclusion in regard to appellants' assertion that the nucleic acid molecules set forth in claim 1 are useful as a molecular marker or probe. It is not seen that the one data point that may be provided by using the

uncharacterized nucleic acid molecule of claim 1 as a molecular marker or probe represents a substantial use.

Further, we understand appellants' position to be that a compound would be patentable if it was adequately described in the specification and was not disclosed or suggested in the prior art. This standard, however, is not the one set by Congress, which requires that a patentable invention also be useful and fully enabled, nor is it the standard that has been consistently applied by the courts.

Not only is appellants' proposed utility standard contrary to controlling case law, but there are reasons to expect that it would hurt – rather than help – the microarray industry. Under appellants' standard, any naturally occurring gene or polypeptide, and fragments thereof, would be held to have patentable utility based on its use in generating expression data. The practical effect of this standard would be that making a microarray with, e.g., 1000 genes represented on it would require investigating the patent status of each oligonucleotide on the microarray. Not only that, but since appellants assert that their reasoning supports the utility of gene and polypeptide fragments, all of the subsequences of each of the genes or polypeptides would have to be checked to ensure that it was not the subject of someone else's patent.

For each of the genes or polypeptides (or fragments thereof) that was the subject of a patent claim held by someone else, a license would have to be negotiated – potentially thousands of such negotiations for the finished product. These transaction costs would have to be incurred for each new product that an

aspiring microarray manufacturer wished to market. The industry gridlock likely to result from this scenario has been termed a "tragedy of the anticommons":⁷

By conferring monopolies in discoveries, patents necessarily increase prices and restrict use—a cost society pays to motivate invention and disclosure. The tragedy of the anticommons refers to the more complex obstacles that arise when a user needs access to multiple patented inputs to create a single useful product. Each upstream patent allows its owner to set up another tollbooth on the road to product development, adding to the cost and slowing the pace of downstream biomedical innovation.

Heller, page 698.

The Supreme Court has warned against allowing too many tollbooths on the road to innovation:

Patents . . . are meant to encourage invention by rewarding the inventor with the right, limited to a term of years fixed by the patent, to exclude others from the use of his invention. . . . But in rewarding useful invention, the "rights and welfare of the community must be fairly dealt with and effectually guarded." Kendall v. Winsor, 21 How. 322, 329 (1859).... To begin with, a genuine "invention" or "discovery" must be demonstrated "lest in the constant demand for new appliances the heavy hand of tribute be laid on each slight technological advance in an art."

Sears, Roebuck & Co. v. Stiffel Co., 376 U.S. 225, 230, 140 USPQ 524, 527 (1964).

The basic quid pro quo of the patent system requires disclosure of an invention having substantial utility. Appellants' disclosure in this case does not provide a specific benefit in currently available form, and therefore lacks the substantial utility required by 35 U.S.C. § 101.

⁷ Heller et al., "Can patents deter innovation? The anticommons in biomedical research," Science, Vol. 280, pp. 698-701 (1998). Available online at www.sciencemag.org/cgi/content/full/280/5364/698.


For the foregoing reasons we affirm the rejection of claim 1 under 35 U.S.C. § 101.

Enablement

According to the examiner (Answer, pages 5-6), "since the claimed invention is not supported by either a specific asserted utility or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." This rejection is simply a corollary of the finding of lack of utility. Appellants assert (Brief, bridging paragraph, pages 11-12), this rejection should be reversed for the same reasons set forth in their arguments regarding the rejection under 35 U.S.C. § 101. Thus, our conclusion with respect to the § 101 issue will also apply to this aspect of the § 112 (enablement) issue. On this basis we affirm the rejection of claim 1 under the enablement provision of 35 U.S.C. § 112, first paragraph.

AFFIRMED


William F. Smith
Administrative Patent Judge


Donald E. Adams
Administrative Patent Judge


Eric Grimes
Administrative Patent Judge

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Appeal No. 2003-1135
Application No. 09/565,240

Page 24

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The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

15746-B

Paper No. 21

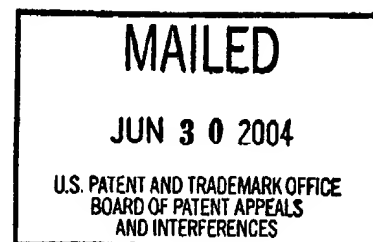
UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte RAGHUNATH V. LALGUDI,
PHILIP W. MILLER and KEITH O'CONNELL

Appeal No. 2003-0996
Application No. 09/540,215

ON BRIEF¹



Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

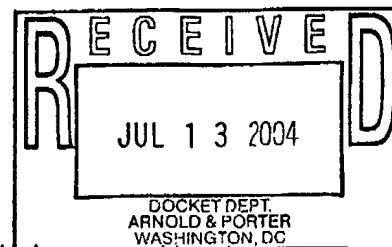
ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1, 2 and 4-7. Claim 1 is illustrative of the subject matter on appeal and is reproduced below:

1. A substantially purified nucleic acid molecule that encodes an algal protein or fragment thereof comprising the nucleic acid sequence of SEQ ID NO: 1.

The examiner does not rely on a reference.



¹ Appellants waived their request for oral hearing. Paper No. 20. Accordingly, we considered this appeal on Brief.

GROUND OF REJECTION

Claims 1, 2 and 4-7 stand rejected under 35 U.S.C. § 101 as lacking utility and § 112, first paragraph, for lack of enablement based on the finding of lack of utility.

Claims 1, 2 and 4-7 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification that fails to adequately describe the claimed invention.

We affirm the utility rejections under 35 U.S.C. § 101 and § 112, first paragraph and reverse the written description rejection under 35 U.S.C. § 112, first paragraph.

BACKGROUND

The subject matter of the present appeal is directed to expressed sequence tags. "Expressed sequence tags, or ESTs, are short sequences of randomly selected clones from a cDNA (or complementary DNA) library which are representative of the cDNA inserts of these randomly selected clones." Specification, page 3.

According to appellants' specification (page 1), "[t]he present invention relates to nucleic acid sequences from the unicellular green algae, Chlorella vulgaris.^[2]" More particularly, appellants disclose "[t]he present invention provides a substantially purified nucleic acid molecule having a nucleic acid

² We note that while claim 2 on appeal is limited to a nucleic acid molecule that comprises SEQ ID NO: 1 and encodes a Chlorella vulgaris protein or fragment thereof, claim 1 on appeal is much broader in scope and encompasses a nucleic acid sequence that encodes any "algal protein or fragment" and comprises the sequence set forth in SEQ ID NO: 1.

sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 3,519." Specification, page 12.

The original claims filed with the application were directed to nucleic acid molecules that comprise a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1 – 3,519. On July 3, 2001 (Paper No. 5), the examiner entered a Restriction requirement into the record. According to the examiner (id. at page 3), "[e]xamination will be restricted to only the elected sequences. For the instant application, the nucleic acid sequences are considered to be complex and thus, election of a single SEQ ID Number is required." In response, appellants elected SEQ ID NO: 1. Paper No. 7, page 2.

CLAIM CONSTRUCTION

As set forth above, claim 1 on appeal is drawn to a substantially purified nucleic acid molecule that encodes an algal protein or fragment thereof comprising the nucleic acid sequence of SEQ ID NO: 1. According to appellants' specification (page 14), the term "substantially purified" refers

to a molecule separated from substantially all other molecules normally associated with it in its native state. More preferably a substantially purified molecule is the predominant species present in a preparation. A substantially purified molecule may be greater than 60% free, preferably 75% free, more preferably 90% free, and most preferably 95% free from the other molecules (exclusive of solvent) present in the natural mixture. The term "substantially purified" is not intended to encompass molecules present in their native state.

As we understand the subject matter of claim 1 the transitional term "comprising" does not allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequence set forth in SEQ ID NO: 1, but instead only allows for the

addition of nucleotides or other molecules³ at either end of the nucleotide sequence.

The preamble of claim 1 also recites that the claimed nucleic acid molecule "encodes an algal protein or fragment thereof." This phrase, however, merely recites an inherent function expected for the nucleotide sequence of the recited SEQ ID NO; since the recited sequence was isolated as an EST from Chlorella vulgaris C-265⁴, it would be expected to encode (part of) an algal protein. Since the introductory phrase does not further limit the invention defined by the body of the claim, it is irrelevant to construction of the claim. See IMS Technology, Inc. v. Haas Automation, Inc., 206 F.3d 1422, 1434, 54 USPQ2d 1129, 1137 (Fed. Cir. 2000) ("If the preamble adds no limitations to those in the body of the claim, the preamble is not itself a claim limitation and is irrelevant to proper construction of the claim.").

Accordingly, for the purposes of our review, we interpret the claimed invention as drawn to a nucleic acid molecule, separated from substantially all other molecules normally associated with it in its native state, that comprises a nucleotide sequence of SEQ ID NO: 1, with or without any preceding or trailing nucleotides, or other molecules.

³ According to appellants' specification (page 15), "agents of the present invention may be labeled with reagents that facilitate detection of the agent (e.g., fluorescent labels, ... chemical labels, ... [and] modified bases...."

⁴ As set forth on page 109 of the specification "[t]he cDNA library LIB191 is prepared from the cultures of the eukaryotic green microalgae Chlorella vulgaris C-265." At page 110 of the specification, appellants disclose that "[t]he ESTs of the present invention are generated by sequencing initiated from the 5' end of each cDNA clone."

DISCUSSION

Utility

The starting point for determining whether the nucleic acid molecule of claim 1⁵ possesses utility under 35 U.S.C. § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). As set forth in Brenner, at 534-35, 148 USPQ at 695⁶,

the basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until [an invention] is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

In considering the issues presented in this appeal, special attention must be paid to the Brenner court's statement that a patent should issue only when an invention possesses "substantial utility," i.e., "where a specific benefit exists in currently available form." Whether a claimed invention is useful under 35 U.S.C. § 101 is a question of fact. Cross v. Iizuka, 753 F.2d 1040, 1044 n.7, 224 USPQ 739, 742 n.7 (Fed. Cir. 1985).

⁵ According to appellants (Brief, page 3), "[t]he patentability of claims 1, 2 and 4-7 is addressed in Sections 8.A through 8.D...." We interpret this statement to mean that claims 1, 2 and 4-7 stand or fall together. Accordingly, we limit our discussion to representative independent claim 1. Claims 2 and 4-7 will stand or fall together with claim 1. In re Young, 927 F.2d 588, 590, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991).

⁶ In discussing the issue of utility under 35 U.S.C. § 101, the Federal Circuit and the Court of Customs and Patent Appeals since Brenner, have used the phrases "substantial utility" and "practical utility" interchangeably. See e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1563-64, 39 USPQ2d 1895, 1898-1899 (Fed. Cir. 1996) ("It is well established that a patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed.").

At issue in Brenner was a claim to “a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced.” Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that “where a claimed process produces a known product it is not necessary to show utility for the product.” Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be “useful,” that “simple, everyday word can be pregnant with ambiguity when applied to the facts of life.” Id. at 529, 148 USPQ at 693. Thus,

[I]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the “new and useful” phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man’s grasp and where little or nothing is wholly beyond the pale of “utility”—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.⁷

The Court, finding “no specific assistance in the legislative materials underlying § 101,” based its analysis on “the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the

⁷ The invention at issue in Brenner was a process, but the Court expressly noted that its holding “would apply equally to the patenting of the product produced by the process.” Id. at 535, 148 USPQ at 695-96.

other.” Id. at 532, 148 USPQ at 695. The Court concluded that “[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.” Id. at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant's argument that attenuating the requirement of utility “would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge.” The Court noted that, while there is value to encouraging disclosure, “a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development.” Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not “mean to disparage the importance of contributions to the fund of scientific information short of the invention of something ‘useful,’” and that it was not “blind to the prospect that

what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroidal research and in the application of steroidal materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" Id. at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. Id. "[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there." Id.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in cancer chemotherapy." Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were "relevant to the treatment of humans and [were] not to be disregarded," id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that "[it] is axiomatic that an invention cannot be considered 'useful,' in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious." Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court "perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for

the compound in question.” Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by “marshal[ling] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds ..., analogous to the benefit provided by the showing of an in vivo utility.” Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be “useful” is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every “use”

that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is “substantial”, i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner’s standard has been interpreted to mean that “vague, general disclosures or arguments of ‘useful in research’ or ‘useful as building blocks of value to the researcher’” would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a “plastic-like” polypropylene capable of being pressed into a flexible film was held to show that the applicant was “at best ... on the way to discovering a

practical utility for polypropylene at the time of the filing," but not yet there.

Ziegler, at 1203, 26 USPQ2d at 1605.

On this record, appellants assert (Brief, bridging paragraph, pages 5-6, footnotes omitted),

The instant specification describes multiple utilities for the present invention, including as probes in an array, to screen for polymorphisms, for gene mapping, and expressing protein for generating antibodies, etc. ... [in addition to] determining the [e]xpression [r]esponse of a green algae as a function of the mRNA levels expressed by the cells ... to identify polymorphisms, in addition to their use as molecular markers.

We note, however, that the specification does not specifically disclose how to use a nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO: 1. To the contrary, the specification describes the aforementioned utilities as applicable to all of the nucleic acid molecules set forth in SEQ ID NO: 1 through SEQ ID NO: 3,519. See e.g., specification, pages 12-13. Stated differently, the specification fails to disclose, with any degree of specificity, the utility of a nucleic acid molecule as claimed.

Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal, i.e., identification and detection of polymorphisms and use as probes or as a source for primers. We shall focus on these asserted utilities first and then address the other arguments set forth in the briefing.

a. Polymorphisms

This utility is discussed at pages 93-101 of the specification in terms of what polymorphisms are and how one would go about determining the existence

of a polymorphism. The discussion in this portion of the specification, however, is not specific to the nucleotide molecule set forth in claim 1. To the contrary, according to appellants' specification (e.g., page 94, lines 4-5), "one or more of the [3,519] EST nucleic acid molecules (or a sub-fragment thereof) may be employed as a marker nucleic acid molecule to identify ... polymorphism(s)."

The specification does not explain why any of the 3,519 nucleic acid molecules disclosed in the specification, or more specifically a nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO: 1 would in fact be useful in detecting polymorphisms. Rather, appellants argue (Brief, page 7), "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." In other words, appellants' position is that a nucleic acid by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. See e.g., Brief, page 10. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by a nucleic acid, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage. As the examiner explains (Answer, page 11), appellants' specification defines

"polymorphism" as

a "variation or difference in the sequence of the gene or its flanking regions that arises in some members of a species." (page 94). It follows from this definition that if there is no "variation or difference in the sequence of the gene or its flanking regions" among "members of a species," then no polymorphism exists, i.e. a polymorphism is absent, in this region of the genome.

According to the examiner (Answer, page 10), "the presence or absence of any of the claimed nucleotide sequences in a sample (or polymorphisms thereof) has no meaning absent some correlation to an immediate benefit." In this regard, the examiner finds (Answer, page 11), appellants' specification "does not disclose whether the claimed nucleic acid molecules can, in fact, be used to detect any polymorphism whatsoever. Thus, the specification leaves open the possibility that there may be no polymorphism to detect." According to the examiner (Answer, page 12),

[t]he specification generally teaches using the claimed polynucleotides to identify a polymorphism, but fails to teach that a polymorphism could in fact be detected, or a specific polymorphisms that could be detected. The specification generally teaches using a polymorphism, detectable with the claimed nucleic acid molecules, as a molecular marker for a linked trait of interest, but fails to teach either the polymorphism or the trait of interest.

According to the examiner (Answer, page 13), "the specification fails to identify even one specific polymorphism that can be detected with the claimed nucleic acid molecule, the specification fails to show any specific correspondence between the disclosed general utility and the claimed subject matter, regardless of any specific application requiring detection of polymorphisms." Accordingly the examiner finds (id.), "using the claimed invention to first determine whether or

not the claimed nucleic acid molecule can, in fact, detect a polymorphism is to determine whether or not the claimed invention has a utility that requires detecting a polymorphism, i.e. it is 'use testing' and not substantial."

In contrast, at the other end of the "utility spectrum" would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene from which the nucleic acid is derived has in the development and/or phenotype of the plant. Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the gene and its role in the plant's development and/or phenotype lies the line between "utility" and "substantial utility." We need not draw the line or further define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.⁸

b. Probes or source of primers

Appellants assert that the "specification discloses that the claimed nucleic acid molecules can be used ... to isolate nucleic acid molecules of other plants such as soybean, alfalfa, Arabidopsis, barley, maize, etc." Brief, page 8, footnote omitted. While that may be true, it begs the question of what substantial use such nucleic acid molecules would have? Again, the present specification does not attribute any property in terms of plant trait, or phenotype to the nucleic acid molecule set forth in claim 1. In the absence of such information, using the

⁸ For the foregoing reasons, we disagree with appellants' assertion (Brief, page 3) that the claimed nucleic acid molecule provides "at least one specific benefit to the public, for example the ability to identify the presence or absence of a polymorphism in a population of algae."

claimed molecule to isolate other molecules, which themselves lack substantial utility, does not represent a substantial utility.⁹

Appellants also assert that the claimed nucleic acid molecule may be used in a "chromosome walk." Brief, page 9. According to appellants (Brief, page 9),

The claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter that is active in green algae. ... Random nucleic acid molecules are not similarly suitable. ... Furthermore, even if a random nucleic acid molecule provided a better starting point than the claimed nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules.

As we understand this argument, the claimed nucleic acid may be useful in searching for promoters that are active in green algae. The specification, however, fails to demonstrate that a nucleic acid molecule as set forth in claim 1 would be useful in obtaining a successful result from such a search.

According to the examiner (Answer, page 15), "the specification fails to disclose any characteristics of the corresponding promoter, or any other promoter within 'chromosome walking' distance; neither structural characteristics, by which the promoter might be identified, nor functional characteristics, by which a specific and substantial use for the promoter might be determined." By way of example, the examiner argues (Answer, bridging paragraph, pages 16-

⁹ In addition, we note the examiner's assertion (Answer, page 15), "[a]t the time the application had been filed, future experimentation on the part of one skilled in the art would have been required to determine which, if any, other plant species contained nucleic acid molecules that could have been obtained using the claimed invention, and under what experimental conditions."

17), assume

a nucleotide sequence is identified during the chromosome walk as a putative promoter by sequence analysis, is then subcloned into operable linkage with a reporter gene and transfected into an appropriate cell, but found not to express the reporter gene in the cells. This result could mean the putative promoter: is not truly a promoter, i.e. a false positive; is not the corresponding promoter; or is incomplete, i.e. lacked additional sequence elements required for promoter activity in the seed pod cells.

According to the examiner (Answer, page 11), appellants merely isolated the claimed nucleic acid molecule, “[t]hey have not tested, evaluated, or calibrated the claimed nucleotide sequence for any particular use.”

We recognize appellants’ argument (Brief, page 9), “[a]n invention may be ‘less effective than existing devices but nevertheless meet the statutory criteria for patentability.’ Custom Accessories, Inc. v. Jeffrey-Allan Indus., 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986).” While we agree with appellants’ statement, we fail to see how it applies to appellants’ claimed invention, wherein there is no evidence or expectation that the claimed nucleic acid molecules would be “effective” at all. In this regard, we remind appellants that an invention does not have utility sufficient to satisfy § 101 until it is “refined and developed” to the point of providing a specific benefit in currently available form. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695.

An invention certainly can have a utility that is shared by other compounds or compositions. Take, for example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful

as analgesics. On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

c. Other Arguments

Upon review of the record, we agree with the examiner that further experimentation would be required to use the claimed nucleic acid molecule “to detect the presence of and/or identify polymorphisms, as hybridization probes in an array for expression profiling, express proteins for generating antibodies, to screen for compounds to determine the effect of the compound on a population of green algae.” Answer, bridging paragraph, pages 7-8.

As to the use of the claimed nucleic acid in microarrays (see e.g., Brief, page 6, n. 3), the examiner finds (Answer, bridging paragraph, pages 8-9), “[a]ppellants are not claiming microarrays or collections of nucleotides and the specification does not associate the claimed sequence with any trait of interest.” According to the examiner (Answer, page 9),

[c]ontrary to [a]ppellants’ assertions, further experimentation is required to identify a “real world use.” For example, a negative hybridization result (which is already a further experimentation) to

such a screen tells what the nucleic acid is not and cannot be used for[;] and a positive result to such a screen requires even further experimentation to determine what, if anything, such a change means. Therefore, the claimed nucleic acid molecule does not provide an immediate benefit except providing a starting point for an artisan to further experiment in order to arrive at the point of immediate "real world" use.

Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. In regard to microarrays, we find that the asserted utility of the claimed nucleic acid—as one component of an assay for monitoring gene expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form. We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid molecule set forth in claim 1. However, the specification provides no guidance that would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification simply provides no guidance regarding what the specific information derived from a gene expression experiment would mean in the context of a nucleic acid molecule as set forth in claim 1.

To highlight the examiner's assertion (Answer, page 9), suppose, for example, that a researcher found that expression of the nucleic acid molecule set forth in claim 1 was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. Maybe the meaning in a change in expression would depend on other factors, but again the specification provides

no hint as to what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), the degree of increase? The specification simply provides no guidance as to how to interpret the results that might be seen using the nucleic acid molecule of claim 1 in a gene expression assay.

In effect, appellants' position is that the claimed nucleic acids are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the present case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, because even if used in gene expression assays, the specification does not disclose how to use the specific gene expression data in the context of the nucleic acid molecule of claim 1.

Assuming arguendo, that a generic gene expression assay - one based on monitoring expression of thousands of uncharacterized nucleic acids - would

provide a useful tool for, e.g., drug discovery, it does not follow that each one of the nucleic acids represented in the assay individually has patentable utility. Although each nucleic acid in the assay contributes to the data generated by the assay overall, the contribution of a single nucleic acid - its data point - is only a tiny contribution to the overall picture. The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently available form. Providing a single data point among thousands or millions, even if the thousands or millions of data points collectively are useful, does not meet this standard. The Supreme Court noted that the patent system contemplates a basic quid pro quo: in exchange for the legal right to exclude others from his invention for a period of time, an inventor discloses his invention to the public. See Brenner, 383 U.S. at 534, 148 USPQ at 695. The Brenner Court held that the grant of patent rights to an applicant is justified only by disclosure of an invention with substantial utility – a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the applicant has not met his side of the bargain, and has not provided a disclosure sufficient to justify a grant of the right to exclude others. See id.

We reach the same conclusion in regard to appellants' assertion that the nucleic acid molecule set forth in claim 1 is useful as a molecular marker or probe. It is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of claim 1 as a molecular marker or probe represents a substantial use.

Appellants argue that ESTs have real world value as seen from the "growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs." Brief, page 11. Since appellants fail to provide any suggestion on which use of ESTs this industry is premised on, we can only assume that appellants are referring to the potential usefulness of EST databases, clone sets or microarrays. Suffice it to say, the claims on appeal are not directed to EST databases, clone sets and/or microarrays. Again, it is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of claim 1 in such devices represents a substantial use.

Further, we understand appellants' position to be that a compound would be patentable if it was adequately described in the specification and was not disclosed or suggested in the prior art. This standard, however, is not the one set by Congress, which requires that a patentable invention also be useful and fully enabled, nor is it the standard that has been consistently applied by the courts.

Not only is appellants' proposed utility standard contrary to controlling case law, but there are reasons to expect that it would hurt – rather than help –

the microarray industry. Under appellants' standard, any naturally occurring gene, and fragments thereof, would be held to have patentable utility based on its use in generating expression data. The practical effect of this standard would be that making a microarray with, e.g., 1000 genes represented on it would require investigating the patent status of each oligonucleotide on the microarray. Not only that, but since appellants assert that their reasoning supports the utility of gene fragments, all of the subsequences of each of the genes would have to be checked to ensure that it was not the subject of someone else's patent.

For each of the genes (or fragments thereof) that was the subject of a patent claim held by someone else, a license would have to be negotiated – potentially thousands of such negotiations for the finished product. These transaction costs would have to be incurred for each new product that an aspiring microarray manufacturer wished to market. The industry gridlock likely to result from this scenario has been termed a “tragedy of the anticommons”:¹⁰

By conferring monopolies in discoveries, patents necessarily increase prices and restrict use—a cost society pays to motivate invention and disclosure. The tragedy of the anticommons refers to the more complex obstacles that arise when a user needs access to multiple patented inputs to create a single useful product. Each upstream patent allows its owner to set up another tollbooth on the road to product development, adding to the cost and slowing the pace of downstream biomedical innovation.

Heller, page 698.

¹⁰ Heller et al., “Can patents deter innovation? The anticommons in biomedical research,” Science, Vol. 280, pp. 698-701 (1998). Available online at www.sciencemag.org/cgi/content/full/280/5364/698.

The Supreme Court has warned against allowing too many tollbooths on the road to innovation:

Patents . . . are meant to encourage invention by rewarding the inventor with the right, limited to a term of years fixed by the patent, to exclude others from the use of his invention. . . . But in rewarding useful invention, the "rights and welfare of the community must be fairly dealt with and effectually guarded." Kendall v. Winsor, 21 How. 322, 329 (1859).... To begin with, a genuine "invention" or "discovery" must be demonstrated "lest in the constant demand for new appliances the heavy hand of tribute be laid on each slight technological advance in an art."

Sears, Roebuck & Co. v. Stiffel Co., 376 U.S. 225, 230, 140 USPQ 524, 527 (1964).

We note that the examiner acknowledges appellants' assertion (Brief, page 6, n. 2), it "is irrelevant whether the corresponding mRNA or polypeptide have utility because [a]pplicants are not relying on utility of the mRNA or polypeptide to establish utility of the claimed nucleic acid molecules." Answer, page 7. Nevertheless, the examiner asserts (Answer, bridging sentence, pages 8-9), "[t]he [B]rief does not dispute that no open reading frame (ORF), no encoded protein, nor any biological activity for the encoded protein has been disclosed for SEQ ID Number 1."

The basic quid pro quo of the patent system requires disclosure of an invention having substantial utility. On reflection, we find appellants' disclosure in this case does not provide a specific benefit in currently available form, and therefore lacks the substantial utility required by 35 U.S.C. § 101.

For the foregoing reasons we affirm the rejection of claim 1 under 35 U.S.C. § 101. As discussed supra, claims 2 and 4-7 fall together with claim 1.

Enablement

According to the examiner (Answer, page 5), "since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." This rejection is simply a corollary of the finding of lack of utility. Appellants assert (Brief, page 12), "[t]he arguments stated above regarding ... [the rejection under 35 U.S.C. § 101]." Thus, our conclusion with respect to the § 101 issue will also apply to this aspect of the § 112 (enablement) issue. On this basis we affirm the rejection of claim 1 under the enablement provision of 35 U.S.C. § 112, first paragraph. As discussed supra, claims 2 and 4-7 fall together with claim 1.

Written description

The examiner rejected claims 1, 2 and 4-7 under 35 U.S.C. § 112, first paragraph, for lack of adequate written description, reasoning (Answer, pages 5-6) that

[c]laim 1 is directed to a nucleic acid molecule "that encodes an algal protein or fragment thereof comprising." The specification fails to describe any open reading frames, start/stop codons, or encoded proteins for SEQ ID Number 1. As such, these nucleic acid molecules are not described. At best, the SEQ ID Number may include a sequence encoding a fragment but not a full length protein.

The use of the term "comprising" is interpreted to encompass full length proteins and gene sequences that have not been disclosed or identified. The common structural features of these encoded plant proteins or fragments are not disclosed and thus the claimed subject matter cannot be considered as being described.

The specification describes only SEQ ID Number 1 and no longer sequences containing them. One can only envision the particular sequence disclosed and cannot envision any encoded protein sequence or larger sequences in which the claimed SEQ ID Number 1 is embedded.

As we understand it, the examiner's rejection has two bases. First, the claimed nucleic acids are not adequately described because the preamble of claim 1 states that the each of the nucleic acids "encodes an algal protein or fragment thereof," and the specification does not describe any encoded proteins.

We will not sustain the rejection on this basis. The claims are directed to nucleic acids, not proteins, and the specification describes the sequence of SEQ ID NO: 1, which defines the scope of the claimed nucleic acid molecule. In addition, as we have construed the claims, the phrase that the examiner objects to ("encodes an algal protein or fragment thereof") has no patentable weight because it merely recites an inherent property that is expected for the claimed nucleic acids, based on the method by which they were isolated.

The second basis of the rejection, as we understand it, is that because of the transitional phrase "comprising", the claims encompass a large genus of nucleic acid molecules, which are not adequately described by SEQ ID NO: 1 as recited in the claim. See the Examiner's Answer, pages 18-22. Apparently, the examiner is of the opinion that the claimed invention should be limited to SEQ ID NO: 1.

In response, Appellants argue that "[t]he fact that the claims at issue are intended to cover molecules that include the recited sequences joined with

additional sequences does not mean that [a]pplicants were any less in possession of the claimed nucleic acid molecules.” Appeal Brief, page 16, footnote omitted.

We have interpreted the claims to allow for the addition of nucleotides or other molecules at either end of the nucleotide sequence set forth in SEQ ID NO: 1, but not to allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequence. See pages 3-4, supra. We agree with appellants that the claims, so interpreted, are supported by an adequate written description in the specification. The fact that the claimed nucleic acid molecules may have other molecules attached to either or both of their 5' or 3' ends does not diminish appellants' adequate written description of a nucleic acids molecule with the sequence set forth in SEQ ID NO: 1, as claimed.

Accordingly, we reverse the rejection of claims 1, 2 and 4-7 for lack of adequate written description.

SUMMARY

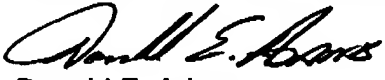
We affirm the utility rejections under 35 U.S.C. § 101 and § 112, first paragraph.

We reverse the written description rejection under 35 U.S.C. § 112, first paragraph.

No time period for taking any subsequent action in connection with this
appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED


William F. Smith
Administrative Patent Judge


Donald E. Adams
Administrative Patent Judge


Eric Grimes
Administrative Patent Judge

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Appeal No. 2003-0996
Application No. 09/540,215

Page 30

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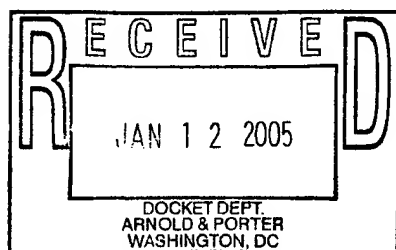
The opinion support of the decision being entered today as not written
for publication and is not binding precedent of the Board.



UNITED STATES PATENT AND TRADEMARK OFFICE

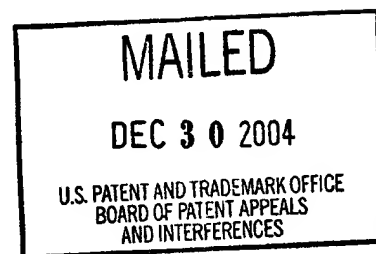
**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte JOSEPH R. BYRUM



Appeal No. 2004-1772
Application No. 09/552,087

ON BRIEF



Before WILLIAM F. SMITH, ADAMS, and GREEN, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the
examiner's final rejection of claims 3, 5-7, 9, 10, and 12-20, which are all the
claims pending in the application.

Claims 3, 7 and 12 are illustrative of the subject matter on appeal and are
reproduced below:

3. A transformed plant cell having a nucleic acid molecule which
comprises:
 - (A) an exogenous promoter region which functions in said cell to
cause the production of a mRNA molecule, wherein said promoter
nucleic acid molecule comprises SEQ ID N0: 1 or a complement
thereof; which is linked to
 - (B) a structural nucleic acid molecule encoding a protein or
peptide; which is linked to

(C) a 3' non-translated sequence that functions in said cell to cause termination of transcription and addition of polyadenylated ribonucleotides to a 3' end of said mRNA molecule.

7. A transformed plant having a nucleic acid molecule which comprises:
 - (A) an exogenous promoter region which functions in a plant cell to cause the production of a mRNA molecule, wherein said promoter nucleic acid molecule comprises SEQ ID NO: 1, or a complement thereof; which is linked to
 - (B) a structural nucleic acid molecule encoding a protein or peptide; which is linked to
 - (C) a 3' non-translated sequence that functions in a plant cell to cause termination of transcription and addition of polyadenylated ribonucleotides to a 3' end of said mRNA molecule.
12. A substantially purified nucleic acid molecule, wherein said nucleic acid molecule comprises a nucleic acid sequence having between 100% and 70% identity with a nucleic acid sequence of SEQ ID NO: 1 or a complement thereof.

No prior art is relied upon in support of the examiner's position.

GROUND OF REJECTION

Claims 3, 5-7, 9-10 and 12-20 stand rejected under 35 U.S.C. § 101 as lacking utility and § 112, first paragraph, for lack of enablement based on the finding of lack of utility.

Claims 12-19 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification fails to provide an adequate written description of the claimed invention.

We reverse the written description rejection, and remand the application to the examiner for further consideration of the utility and enablement rejections.

DISCUSSION

Written Description:

The examiner rejected the claims as inadequately described, on the basis that the claimed nucleic acids

comprise SEQ ID NO: 1 or a nucleic acid related to SEQ ID NO: 1 by a particular range of identity (i.e. 100% to 80% identity, as in claim 13)¹. This genus is sufficiently broad so as to encompass a multitude of variants of SEQ ID NO:1, as well as any full length coding sequence, mRNA, promoter, or genomic DNA of which SEQ ID NO: 1 is a portion, or of which the recited polynucleotides with identity to SEQ ID NO: 1 are portions. This large genus is represented in the specification by one species, a nucleic acid consisting of SEQ ID NO: 1.

Answer, bridging paragraph, pages 8-9 .

We will reverse this rejection. The written description requirement of 35 U.S.C. § 112, first paragraph, does not require a description of the complete structure of every species within a chemical genus. See Utter v. Hiraqa, 845 F.2d 993, 998, 6 USPQ2d 1709, 1714 (Fed. Cir. 1988) ("A specification may, within the meaning of 35 U.S.C. § 112, ¶ 1, contain a written description of a broadly claimed invention without describing all species that claim encompasses.").

The Federal Circuit has held that "[a] description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which

¹ While the examiner refers to claim 13, which depends from claim 12, we note as illustrated above, that claim 12 is broader than claim 13, in that it relates to a "sequence having between 100% and 70% identity with a nucleic acid sequence of SEQ ID NO: 1 or a complement thereof."

features constitute a substantial portion of the genus.” University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Our appellate reviewing court has also held that the complete structure of a claimed DNA is not necessarily required. The court adopted the standard that “the written description requirement can be met by ‘show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.” Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 1324, 63 USPQ2d 1609, 1613 (Fed. Cir. 2002) (emphasis omitted, alterations in original).

With respect to the claimed sequences that have 70% to 100% identity with SEQ ID NO:1, the Lilly court held that a genus could be described via “recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.” Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406. The Enzo court held that such a description could take the form of “complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.” 296 F.3d at 1324, 63 USPQ2d at 1613. In this case, the complete structure of SEQ ID NO:1 has been described, and the nucleic acids of the claimed genus share 70 or more percent identity with the structure of SEQ ID NO:1. Thus, the structural features that are common to the genus make up 70% of the structure

of the claimed polypeptides. The examiner has not adequately explained why this degree of structural similarity is inadequate to "constitute a substantial portion of the genus," as required by Lilly.

Accordingly, we reverse the rejection of claims 12-19 under 35 U.S.C. § 112, first paragraph, as the specification fails to provide an adequate written description of the claimed invention.

Utility:

The issues of whether a disclosure satisfies the "how to use" provision of 35 U.S.C. § 112, and the utility requirement of 35 U.S.C. § 101, are closely related. See In re Swartz, 232 F.3d 862, 863, 56 USPQ2d 1703 (Fed. Cir. 2000), Process Control Corp. v. HydReclaim Corp., 190 F.3d 1350, 1358, 52 USPQ2d 1029, 1034 (Fed. Cir. 1999), Newman v. Quigg, 877 F.2d 1575, 1581, 11 USPQ2d 1340, 1345 (Fed. Cir. 1989). Under the utility requirement, our appellate reviewing court, has held that it makes no sense to require claims to set forth inventions that satisfy all the disclosed objectives, but that "[w]hen a properly claimed invention meets at least one stated objective, utility under § 101 is clearly shown." Raytheon Co. v. Roper Corp., 724 F.2d 951, 958, 220 USPQ 592, 598 (Fed. Cir. 1983).

As set forth in In re Langer, 503 F.2d 1380, 183 USPQ 288 (CCPA 1974), emphasis in original:

As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of Section 101 for the entire claimed subject matter unless there is reason for one skilled in the art to question

the objective truth of the statement of utility or its scope. Assuming that sufficient reason to question the statement of utility and its scope does exist, a rejection for lack of utility under Section 101 will be proper on that basis; such a rejection can be overcome by suitable proofs indicating that the statement of utility and its scope as found in the specification are true. Cf. In re Marzocchi, 58 CCPA 1069, 1073, 439 F.2d 220, 223, 169 USPQ 367, 369 (1971) (involving the enablement requirement of 35 U.S.C. 112, first paragraph).

According to the examiner (Answer, page 6), "[t]here has been no specific assertion that in fact SEQ ID NO: 1 is a promoter, aside from the claims."

Contrary to the examiner's assertion, however, appellant's specification does set forth a statement of utility that corresponds in scope to the subject matter claimed. Specifically, appellant discloses (specification, page 16), "[a]nother class of agents of the present invention are nucleic acid molecules having promoter regions or partial promoter regions, including those located within SEQ ID NO: 1...." As set forth in Raytheon, "[w]hen a properly claimed invention meets at least one stated objective, utility under § 101 is clearly shown."

Similarly, as set forth in Johns Hopkins Univ. v. CellPro Inc., 152 F.3d 1342, 1361, 47 USPQ2d 1705, 1714 (Fed. Cir. 1998), "[t]he enablement requirement is met if the description enables any mode of making and using the invention."

Therefore, it is the examiner's initial burden to establish that those skilled in this art would question the objective truth of the asserted utility. See In re Brana, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 ("Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence."). In our opinion, the examiner has not provided sufficient evidence to

show that one of ordinary skill in the art would reasonably doubt that a nucleic acid molecule comprising SEQ ID NO: 1 would not have utility as a promoter as disclosed in appellants' specification.

To the contrary, the examiner has simply asserted (Answer, page 5) that "further experimentation would be required to reasonably confirm that SEQ ID NO: 1, or its complement, or fragments of either would function as a promoter as required by the claims. The specification does not provide any guidance as to the use of SEQ ID NO: 1, its complement or fragments thereof as promoters." Based on this assertion, the examiner concludes, "[t]he use of ... SEQ ID NO: 1 as a promoter is not a specific or substantial utility since further experimentation would be required to confirm that in fact SEQ ID NO: 1 has the ability to cause the production of an mRNA molecule...." Answer, page 6. While appellant has disclosed the characteristics of promoters within the scope of the claimed invention at pages 16-17 of the specification, the examiner fails to address this section of appellant's specification, or to establish a factual basis on this record to support the assertion that SEQ ID NO: 1 does not contain a promoter element.

According to the examiner (id.), "one would have to determine if the ... [promoter] is tissue specific or constitutive, for example, or if it is an inducible promoter, and under what circumstances it is induced or repressed in order to make use of the claimed plants." The examiner finds (id.), "[e]ach of these determinations is highly unpredictable, from the determination ... of the type of promoter it may be to the determination of fragments of the promoter that confer

promotion activity.” The examiner, however, fails to establish a factual basis on this record to support these assertions.

Further, our review of this record is hindered by the examiner’s failure to apply any type of claim construction to the claims now before us on appeal. In this regard, we note that claims 3 and 7, as well as the claims that depend from these claims, require in part “(A)” of each claim “an exogenous promoter region which functions ... to cause the production of a mRNA molecule.” According to part “(A)” of these claims the promoter “comprises SEQ ID NO: 1 or a complement thereof....” We find no clear disclosure in the specification that SEQ ID NO: 1 is capable of functioning as a promoter region in plant cells to cause the production of a mRNA molecule. As we understand it, part “(A)” of these claims is open to at least three possible interpretations:

1. SEQ ID NO: 1 contains a promoter region which does function in plant cells to cause the production of a mRNA molecule,
2. SEQ ID NO: 1 does not contain a “promoter region,” but instead contains a “regulatory element”² that acts in concert with a promoter region operably attached, either 5’ or 3’, to SEQ ID NO: 1, and thereby serves to regulate the expression of a mRNA molecule. For example, SEQ ID NO: 1 is an enhancer regions which is incapable of acts on a promoter, but is insufficient to function in plant cells to cause the production of a mRNA molecule on its own, or
3. SEQ ID NO: 1 contains neither a promoter region nor a regulatory element and simply serves as a filler sequence between the promoter region and a structural nucleic acid molecule, as defined in part “(B)” of these claims. For example, SEQ ID NO: 1 is incapable of functioning in plant cells to cause the production of a mRNA molecule, but instead serves only to

² See e.g. appellant’s specification, page 17.

maintain the proper distance between a promoter and a
"regulatory element."

It may be that the examiner is of the opinion that SEQ ID NO: 1 does not contain a promoter element. Cf. interpretation 3 above. The examiner, however, has not provided a sufficient evidentiary basis on this record to establish that SEQ ID NO: 1 does not contain a promoter or regulatory region, or if it does, why a person of ordinary skill in the art would reasonably doubt that the sequence would not function as a promoter or regulatory region.


For the foregoing reasons we remand the application to the examiner for further consideration. Prior to any further action on the merits, we encourage the examiner to take a step back and reconsider the claimed invention together with appellant's specification and the relevant prior art. In this regard, we remind the examiner as set forth in In re Zletz, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989), "claims must be interpreted as broadly as they reasonably, allow, in order to achieve complete exploration of applicant's invention and its relationship to prior art, so that ambiguities can be recognized, scope and breadth of language explored, and clarification imposed." Accordingly, prior to taking any action on the record, we encourage the examiner to determine the broadest reasonable interpretation of the claimed invention and to include an analysis of this claim construction in any subsequent Office Action. If, after the examiner has evaluated the scope of the claim, the examiner believes that a rejection is necessary, the examiner should include on this record, an analysis of the claim construction together with a reasoned, fact-

based analysis of claimed invention together with the evidence necessary to support any such rejection.

In addition, we note that appellant has disclosed and argued that a nucleic acid molecule comprising SEQ ID NO: 1 has a number of utilities, e.g., for identifying the presence or absence of a polymorphism, or as probes for other molecules or as a source for primers (see e.g., Brief, pages 7-11). These issues and arguments, however, bear a close resemblance to those presented in Ex parte Fisher, 72 USPQ2d 1020 (Bd. Pat. App. & Int. 2004) (affirming the rejection of claim 1 under 35 U.S.C. § 101 and § 112, first paragraph.). Accordingly, we encourage both the examiner and appellants to take the opportunity to reconsider their arguments on this record and to take into account the effect, if any, that Fisher may have on the issues under 35 U.S.C. § 101 and § 112, first paragraph.

REVERSED-IN-PART and REMANDED


William F. Smith
Administrative Patent Judge


Donald E. Adams
Administrative Patent Judge


Lora M. Green
Administrative Patent Judge

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Appeal No. 2004-1772
Application No. 09/552,087

Page 11

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The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 26

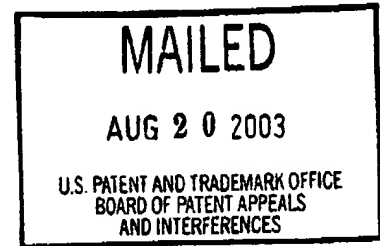
UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte JOSEPH R. BYRUM,
THOMAS J. La ROSA, and
GREGORY R. HECK,

Appeal No. 2002-0078
Application No. 09/206,040

ON BRIEF



Docketed
Due Date 10-20-03
Initial UB

Before STONER, Chief Administrative Patent Judge, and WILLIAM F. SMITH and SCHEINER, Administrative Patent Judges.

WILLIAM F. SMITH, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from an examiner's final rejection of claims 1 through 3, which read as follows:¹

¹ A copy of SEQ ID No. 1 is attached to this opinion.

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AUG 20 2003

WASHINGTON, D.C.

1. A nucleic acid molecule isolated from other nucleic acid molecules and comprising SEQ ID No. 1 or its complement.
2. A nucleic acid molecule consisting of SEQ ID No. 1 or its complement.
3. A nucleic acid molecule isolated from other nucleic acid molecules and consisting essentially of SEQ ID No. 1 or its complement.

Claims 1 through 3 stand rejected under 35 U.S.C. § 101 (utility) and § 112, first paragraph (enablement). Claims 1 and 3 also stand rejected under 35 U.S.C. § 112, first paragraph (written description). We affirm the utility and enablement rejections and do not reach the merits of the written description rejection. Since our reasons for concluding that the claims lack patentable utility differ substantially from those advanced by the examiner, we denominate our affirmance as a new ground of rejection under 37 CFR § 1.196(b).

Background

The nucleic acid molecule set forth in SEQ ID No. 1 is stated to be an expressed sequence tag (EST) obtained from soybean plant material. Specification, page 14 ("The present invention provides soybean ESTs . . ."), Appeal Brief, page 2 ("The invention is directed to nucleic acid molecules reciting the sequence of an expressed sequence tag . . ."). ESTs are "short sequences of randomly selected clones from a cDNA (or complementary DNA) library which are representative of the cDNA inserts of these randomly selected clones." Specification, page 1. As explained in Examples 1 and 2 of the specification, the claimed EST was obtained from a cDNA library prepared

from young soybean seeds collected from young pods.² The cDNA library from which the nucleic acid molecule set forth in SEQ ID No. 1 was isolated has been designated LIB3049. Specification, page 18.

The three claims before us for review define the claimed nucleic acid molecule as comprising, consisting of, or consisting essentially of SEQ ID No. 1 or its complement. Appellants explain that a nucleic acid molecule is said to be the 'complement' of another nucleic acid molecule if it exhibits complete complementarity, stating "[a]s used herein, molecules are said to exhibit 'complete complementarity' when every nucleotide of one of the molecules is complementary to a nucleotide of the other." Specification, page 16. However, appellants back away from this absolute definition of "complement" stating that "[d]epartures from complete complementarity are permissible, as long as such departures do not completely preclude the capacity of the molecules to form a double stranded structure." Specification, page 17.

The specification sets forth a number of utilities for the nucleic acid molecule of SEQ ID No. 1 which are summarized by the examiner as follows:

The utilities disclosed for the EST of SEQ ID NO: 1 or fragment thereof, or a nucleic acid molecule comprising same are:

² The record contains conflicting statements in regard to the source of the cDNA library from which the claimed EST was isolated. Example 1 states that the cDNA library was obtained from young seeds collected from young pods while page 24 of the specification states that the nucleic acid molecules of the present invention "were isolated from pods and seeds." (Emphasis added). Appellants summarize their invention at page 2 of the Appeal Brief stating that "[t]he claimed nucleic acid molecules were derived from a cDNA collection prepared from young soybean pods." Thus, it is unclear whether the cDNA library was obtained from young seeds, young pods, or a combination of young seeds and young pods. If prosecution is resumed on this subject matter, appellants should clarify the source of the claimed nucleic acid molecule.

sequences corresponding to the claimed nucleic acid molecule in a genome, and then use as a probe for detecting the polymorphisms, which serve as a molecular marker, either a) for a mutation affecting the expression of a product encoded, at least in part, by the claimed nucleic acid molecule (specification, pages 27-28) or b) for a desirable trait that is genetically linked to the polymorphism (specification, pages 35-36);

- Use of the EST as a probe for detecting a physical map location, e.g. as a marker in in situ hybridization;
- Use as a probe or source of PCR primers either to isolate other nucleic acid molecules (e.g. complete cDNA, protein coding sequence, genomic fragment, promoter, start of a chromosome walk) from the same organism or different organisms, i.e. other plants, or to detect other nucleic acid molecules (e.g. mRNA, chromosomal region, chromosome). Disclosed for the latter, for example, is to detect the mRNA in different tissues or as a measure of protein expression from the mRNA (based on mRNA levels), particularly if there is a mutation (hypothetical) affecting expression;
- Use of the EST as an antisense inhibitor of the corresponding mRNA; and
- Use as a probe to identify or isolate proteins that might bind to the EST sequence.

Examiner's Answer, pages 4-5. In the opinion of the examiner:

Each of these utilities requires additional knowledge about the EST before the EST can be used for a specific purpose, such as: whether there are sequence polymorphisms linked to the gene corresponding to the EST and, if so, their identity; the map location of the corresponding gene; the sequence of the corresponding complete mRNA sequence, protein coding sequence or genomic sequence; the function of the protein encoded by the corresponding mRNA; the identity and phenotype, if any, of a mutation in the corresponding gene; the tissue distribution of the corresponding mRNA and tissue-specific expression levels; etc. The specification does not provide any such information specific to the disclosed EST. Consequently, the disclosed utilities are non-specific utilities, since any of the general disclosed utilities would apply equally to any uncharacterized nucleic acid molecule from soybean in particular, or plants in general.

Examiner's Answer, paragraph bridging pages 5-6.

The examiner concludes:

In Brenner v. Manson, 148 USPQ 689, 696 (US, 1966), the Court held that "Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." The original disclosure lacks any successful conclusion for even one of the vague and general utilities disclosed. Thus, no "substantial" or "real world" utility has been disclosed.

Examiner's Answer, page 6.

Appellants urge that the claims on appeal possess patentable utility under 35 U.S.C. § 101. See, e.g., Appeal Brief, page 19 ("Applicants have disclosed numerous utilities for the claimed nucleic acid molecules, and have submitted evidence proving that the claimed nucleic acid molecules work for at least two of the disclosed utilities."). In presenting their case on appeal, appellants focus on use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism, and their use as probes or as a source for primers. Appeal Brief, pages 11-18.

In support of their position, appellants rely upon the declaration of Dr. Roger C. Wiegand.³ Dr. Wiegand states that "EST databases are useful tools that may be used to select clones for further research, or to compare sequences in the database with other sequences, but the nucleic acid molecules represented by the ESTs themselves have value beyond that associated with their ESTs." Wiegand decl., para. 6. Dr. Wiegand also states that "ESTs are typically used to develop molecular markers,

³ Appellants also refer to a La Rosa declaration in the heading appearing on page 4 of the Appeal Brief. However, the La Rosa declaration is only directed to the deposit of clone designated LIB-3049-003-Q1-E1-H7 with the ATCC.

hybridization probes, amplification primers, and to identify the presence or absence of polymorphisms." Wiegand decl., para. 7. Dr. Wiegand also discusses the results of tests performed with a nucleic acid molecule "having the sequence of SEQ ID No. 1" in regard to its use as a hybridization probe in detection of genetic polymorphism, stating:

19. The results of the northern blots indicate that a nucleic acid molecule having the sequence of SEQ ID NO: 1 can be synthesized and successfully used as a hybridization probe, and that such a molecule will hybridize to a naturally occurring soybean nucleic acid molecule. Accordingly, a nucleic acid molecule having SEQ ID NO: 1 is useful as a hybridization probe for expression profiling or other purposes.

21. I believe that a nucleic acid molecule comprising the EST of SEQ ID NO: 1 possesses the practical utility of being useful for detecting polymorphisms because scientists under my supervision performed Southern blots to test if a synthetic nucleic acid molecule based on SEQ ID NO: 1 would detect polymorphisms. It did.

23. The results of the Southern blots indicate that a nucleic acid molecule having the sequence of SEQ ID NO: 1 can be synthesized and successfully used to detect polymorphisms in soybean chromosomal DNA. Accordingly, a nucleic acid molecule having the sequence of SEQ ID NO: 1 is useful for detecting polymorphisms in order to develop a genetic map, determining if a plant carries the gene for a particular trait, determining the copy number of a particular gene in a plant, or for other purposes.

Wiegand decl., paras. 19, 21, and 23.

In regard to claim construction, the examiner states in the context of setting forth the enablement rejection:

The recitation of "consisting essentially of" in claim 3 has been treated as being equivalent to "comprising", as recited in claim 1. There is nothing on the record to indicate how "consisting essentially of" alters the scope of claim 3 compared to claim 1. Thus, claim 3 would not exclude any embodiment embraced by claim 1.

Examiner's Answer, page 7. The examiner has determined that claims 1 and 3 embrace an "essentially infinite genus of nucleic acid molecules" (Examiner's Answer, page 8) and that the specification does not "teach the maximum length or locations (5' end, 3' end, or both ends, of nucleic acid sequence(s) that could be added to SEQ ID NO: 1, that would not interfere with its disclosed use as a hybridization probe." Id. The examiner is also of the opinion that "[s]ince the claims embrace adding any and all nucleic acid sequences to the core nucleic acid molecule SEQ ID NO: 1, one cannot predict whether or not the additional nucleic acid sequence[s] added would hybridize to a target nucleic acid molecule other than the intended target nucleic acid molecule. When such a situation occurs, and more than one nucleic acid molecule is amplified or detected in hybridization, the skilled artisan would have no information that would allow the desired target nucleic acid molecule to be distinguished from a nucleic acid molecule that was targeted by the added nucleic acid sequences." Examiner's Answer, page 9. The examiner concludes:

Consequently, making the myriad of nucleic acid molecules embraced by the claims and testing the suitability of each for use as a probe or primer for the disclosed utilities in the absence of guidance or examples would require excessive trial and error experimentation due to the unpredictability involved, and would therefore require undue experimentation.

Id.

In reaching the conclusion of undue experimentation, the examiner did not perform an analysis of the so-called Wands factors. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404, (Fed. Cir. 1988). In contrast to the examiner's position,

appellants provide an analysis of the Wands factors in support of their position that the claim are enabled. Appeal Brief, pages 27-36.

The examiner's reasoning in regard to the written description rejection is:

Claims 1 and 3 are drawn to nucleic acid molecules "comprising" or "consisting essentially of" the EST of SEQ ID NO: 1; and therefore to an astronomically large genus of nucleic acid molecules comprising SEQ ID NO: 1 even solely considering nucleic acid sequences and ignoring nucleic acid molecules comprising non-nucleotide moieties such as detectable labels. The specification does not explicitly disclose any nucleic acid molecules that "comprise" or "consist essentially of" SEQ ID NO: 1, other than that of SEQ ID NO: 1 itself (either unlabeled or labeled with a detectable non-nucleotide moiety such as a fluorophor) and the clone from which the sequence was derived. Any additional cDNA sequence that may be present on the clone was not described other than by deposit. No nucleic acid molecules are disclosed wherein the nucleic acid sequence is extended beyond SEQ ID NO: 1, other than solely by implication a larger EST or mRNA comprising SEQ ID NO: 1. However, the specification does not disclose the structure of any such larger nucleic acid molecule or EST or mRNA. The disclosure of the single nucleic acid molecule set forth as SEQ ID NO: 1 does not adequately describe the astronomically large number of possible nucleic acid molecules embraced by claims 1 and 3.

Examiner's Answer, page 10.

Appellants respond that the specification reflects their "possession" of the claimed invention. Appeal Brief, pages 36-41.

Discussion

As always, we begin our analysis by construing the claims as "the name of the game is the claim." In re Hiniker Co., 150 F.3d 1362, 1369, 47 USPQ2d 1523, 1529 (Fed. Cir. 1998)(citing Giles Sutherland Rich, Extent of Protection and Interpretation of Claims--American Perspectives, 21 Int'l Rev. Indus. Prop. & Copyright L. 497, 499 (1990). See also, Panduit Corp. v. Dennison Manufacturing Co., 810 F.2d 1561, 1567-

68, 1 USPQ2d 1593, 1597 (Fed. Cir.), cert. denied, 481 U.S. 1052 (1987) ("Analysis begins with a key legal question--what is the invention claimed? ... Claim interpretation ... will normally control the remainder of the decisional process."). The claim analysis which appears in the Appeal Brief and the Examiner's Answer provides little assistance in our review of the issues presented in this appeal. For example, appellants state "[t]he genus of claimed nucleic acid molecules, i.e., nucleic acid molecules 'comprising,' 'consisting of,' and 'consisting essentially of' SEQ ID No. 1 have been described by the recitation of a 'basic and novel' common structural feature - the nucleotide sequence of SEQ ID No. 1 - which distinguishes them from nucleic acid molecules not in the claimed genus." Appeal Brief, page 4. Appellants have not explained on this record how a nucleic acid molecule which "comprises" the nucleotide sequence of SEQ ID No. 1 differs from a nucleic acid molecule "consisting of" or "consisting essentially of" the nucleotide sequence of SEQ ID No. 1. Appellants' arguments for the most part are couched in vague, non-specific terms such as "the claimed nucleic acid molecules," instead of referring to actual claims and the language used therein. See, e.g., Appeal Brief, page 8, first full paragraph ("Applicants have asserted specific utilities for the claimed nucleic acid molecules...."). Importantly, appellants have not offered any assistance in the Appeal Brief as to how broadly or narrowly they would have the word "complement" construed as it is used in claims 1-3 on appeal.

The one specific statement we find in the Examiner's Answer construing the claims on appeal is contrary to governing precedent and, thus, is in error. The examiner states "[t]he recitation of 'consisting essentially of' in claim 3 has been treated

as being equivalent to 'comprising', as recited in claim 1. There is nothing on the record to indicate how 'consisting essentially of' alters the scope of claim 3 compared to claim 1. Thus, claim 3 would not exclude any embodiment embraced by claim 1."

Examiner's Answer, page 7, fourth full paragraph. The examiner's holding that the transitional phrase "consisting essentially of" is equivalent to the transitional phrase "comprising" is contrary to long established precedent. In re Janakirama-Rao, 317 F.2d 951, 954, 137 USPQ 893, 896 (CCPA 1963) ("The word 'essentially' opens the claims to the inclusion of ingredients which would not materially affect the basic and novel characteristics of appellants' compositions as defined in the balance of the claim, according to the applicable law."). Assuming the examiner is correct in concluding there is "nothing on the record" that would allow the examiner to distinguish between a claim using the transitional phrase "consisting essentially of" and the same claim using the transitional phrase "comprising," we do not find that to be sufficient justification for the examiner to upend decades of precedent. These transitional phrases have defined meanings in the law. The fact that an examiner is having trouble distinguishing the scope of claims 1 and 3 on the basis of the transitional phrases used may, however, be an indication that the claims are indefinite under 35 U.S.C. § 112, second paragraph. In re Hammack, 427 F.2d 1378, 1382, 166 USPQ 204, 208 (CCPA 1970) (Purpose of 35 U.S.C. § 112, second paragraph, "is to provide those who would endeavor, in future enterprise, to approach the area circumscribed by the claims of a patent, with the adequate notice demanded by due process of law, so that they may more readily and

accurately determine the boundaries of protection involved and evaluate the possibility of infringement and dominance.").

Additional ambiguity is injected in the claims by use of the word "complement" and the reference in the claims to SEQ ID No. 1. As discussed above, the specification contains a very strict definition of complement, i.e., every nucleotide of one of the molecules is complementary to a nucleotide of another nucleic acid molecule, while at the same time indicating that the nucleic acid molecules according to the present invention may depart from "complete complementarity." Thus, determining what constitutes a "complement" of the claimed nucleic acid molecules as that word is used in the claims on appeal is problematic.

The reference in the claims to SEQ ID No. 1 is also subject to interpretation as appellants state "[a]n aspect to the present invention is that the nucleic acid molecules of the present invention include nucleic acid molecules that are degenerate of that set forth in SEQ ID No. 1." Specification, page 18. As acknowledged by appellants, "a nucleic acid molecule is degenerate of another nucleic acid molecule when the nucleic acid molecules encode for the same amino acid sequences but comprise different nucleotide sequences." Id. The nucleotide sequence depicted in SEQ ID No. 1 does not indicate the reading frame or contain an assigned amino acid sequence. Without such knowledge, it is unclear how one would consider a given nucleotide sequence to be "degenerate" of that depicted in SEQ ID No. 1. Thus, if the claims on appeal are to be read as encompassing degenerate nucleotide sequences, the determination of the identity of such degenerate molecules would be difficult.

Having a firm understanding of the scope of the claims under review is also necessary in evaluating appellants' rebuttal evidence in regard to the utility rejection. For example, Dr. Wiegand states "the synthetic probe is a true enough copy of SEQ ID No. 1 for use as a probe to demonstrate the utility of nucleic acid molecules characterized by SEQ ID No. 1." Wiegand Declaration, para. 16. (Emphasis added). If one cannot readily determine whether a given nucleotide sequence is within or without the scope of the claims under review, it is difficult to assign weight to evidence which is based upon "a true enough copy of SEQ ID No. 1."

The ability or inability to reasonably ascertain the metes and bounds of a claim is important in determining whether the claim possesses patentable utility under § 101 as all embodiments within a claim must meet the utility requirement. In re Langer, 503 F.2d 1380, 1394, 183 USPQ 288, 299 (CCPA 1974) ("We hold that appellant's evidence of record is insufficient to rebut the prima facie case for lack of utility in the subject matter (other than [preferred species]) recited in these claims."). In similar fashion, it is difficult to determine whether a given claim is enabled throughout its scope without undue experimentation without first knowing the scope of the claim under review. In re Moore, 439 F.2d 1232, 1236, 169 USPQ 236, 238 (CCPA 1971) ("Once having determined that the subject matter defined by the claims is particular and definite, the analysis then turns to the first paragraph of § 112 to determine whether the scope of protection sought is supported and justified by the specification disclosure.") (Emphasis added). The same holds true in considering the written description requirement of the first paragraph of § 112. Enzo Biochem, Inc. v. Gen-Probe, Inc., 296

F.3d 1316, 1327, 63 USPQ2d 1609, 1615 (Fed. Cir. 2002) ("On remand, the court should determine whether a person of skill in the art would glean from the written description, including information obtainable from the deposits of the claimed sequences, subsequences, mutated variants and mixtures sufficient to demonstrate possession of generic scope of the claims.").

Reaching a decision on a record such as this is difficult. However, we do know that the claims on appeal include one discrete and definite embodiment not subject to interpretation, alternative construction, ambiguity or spin of any type, i.e., the precise 469 nucleotide sequence set forth in SEQ ID No. 1 without any preceding or trailing nucleotides.

Thus, we will proceed to a decision on the issues raised in this appeal to the extent that claims 1 through 3 on appeal include the nucleic acid molecule defined by the 469 nucleotide sequence set forth in SEQ ID No. 1 without alteration or any preceding or trailing nucleotides as this is the only subject matter that we can say with certainty is included within each of the claims.

1. Utility.⁴

The starting point for determining whether a nucleic acid molecule having the 469 nucleotide sequence set forth in SEQ ID No. 1 possesses utility under 35 U.S.C.

⁴ Appellants refer to the "Revised Utility Examination Guidelines, 64 Fed. Reg. 71440, 71442" in presenting their case on appeal. See, e.g., Appeal Brief, page 5. Those guidelines were superseded by Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001). Although the Appeal Brief and the Examiner's Answer were prepared after that date, it does not appear that either appellants or the examiner considered the latest version of the guidelines in preparing the briefing in this appeal. Be that as it may, we note that the utility guidelines expressly state that they do not have the force or effect of law, see *id.* at 1098, and our analysis is based instead on controlling precedent. We note, however, that our conclusion is consistent with the utility guidelines.

§ 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). The Court stated "the basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until [an invention] is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.⁵ In considering the issues presented in this appeal, special attention must be paid to the Court's statement that a patent should issue only when an invention possesses "substantial utility," i.e., "where a specific benefit exists in currently available form." Whether a claimed invention is useful under 35 U.S.C. § 101 is a question of fact. Cross v. Iizuka, 753 F.2d 1040, 1044 n.7, 224 USPQ 739, 742 n.7 (Fed. Cir. 1985).

At issue in Brenner was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that

⁵ In discussing the issue of utility under 35 U.S.C. § 101, the Federal Circuit and the Court of Customs and Patent Appeals since Brenner, has used the phrases "substantial utility" and "practical utility" interchangeably. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1963-1964, 39 USPQ2d 1895, 1898-1899 (Fed. Cir. 1996) ("It is well established that a patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed.").

"where a claimed process produces a known product it is not necessary to show utility for the product." Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be "useful," that "simple, everyday word can be pregnant with ambiguity when applied to the facts of life." Id. at 529, 148 USPQ at 693. Thus,

[i]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new and useful" phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of "utility"—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.⁶

The Court, finding "no specific assistance in the legislative materials underlying § 101," based its analysis on "the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other." Id. at 532, 148 USPQ at 695. The Court concluded that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.

⁶ The invention at issue in Brenner was a process, but the Court expressly noted that its holding "would apply equally to the patenting of the product produced by the process." Id. at 535, 148 USPQ at 695-96.

The Court considered and rejected the applicant's argument that attenuating the requirement of utility "would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge." The Court noted that, while there is value to encouraging disclosure, "a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d

936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroidal research and in the application of steroidal materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" Id. at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. See id., 26 USPQ2d at 1606. "[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there." Id., 26 USPQ2d at 1605.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in cancer chemotherapy." Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one

was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were “relevant to the treatment of humans and [were] not to be disregarded,” id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that “[it] is axiomatic that an invention cannot be considered ‘useful,’ in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious.” Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court “perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question.” Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by “marshal[ling] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds . . . , analogous to the benefit provided by the showing of an in vivo utility.” Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be

met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best . . . on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

With these principles in mind we turn to the issues at hand. Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal, i.e., identification and detection of polymorphisms and use as probes or as a source for primers. We shall focus on these asserted utilities first and then address the other arguments set forth in the briefing.

a. Polymorphisms

This utility is discussed at pages 28-35 of the specification in terms of what polymorphisms are and how one would go about determining the existence of a polymorphism. The discussion in this portion of the specification is not specific to the 469 nucleotide molecule depicted in SEQ ID No. 1. Nor does the specification explain why the 469 nucleotide molecule of SEQ ID No. 1 would in fact be useful in detecting polymorphisms. Rather, appellants' argument is that "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." Appeal Brief, page 14. In other words, appellants' position is that an EST by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by an EST, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage and can be viewed to be at the lower end of the utility spectrum. At the high end of the utility spectrum would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene from which the EST is derived has in the development and/or phenotype of the plant. Somewhere between having no knowledge of the gene and its role in the plant's development and phenotype (the present circumstances) and having

complete knowledge of the gene and its role in the plant's development and/or phenotype lies the line between "utility" and "substantial utility." We need not draw the line or further define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.

Dr. Wiegand's declaration does not aid appellants in this aspect of their case. Polymorphism as a utility is discussed primarily in paragraphs 20-23 of the declaration. Two probes were used in Dr. Wiegand's work, "a synthesized nucleic acid molecule based on overlapping oligomers matching SEQ ID No. 1; and a probe derived from the plasmid that carries clone LIB3049-003-Q1-E1-H7, from which SEQ ID No. 1 was determined." Dr. Wiegand concludes that "a nucleic acid molecule having a sequence of SEQ ID No. 1 can be synthesized and successfully used to detect polymorphisms in soybean chromosomal DNA. Accordingly, a nucleic acid molecule having the sequence of SEQ ID NO. 1 is useful for detecting polymorphisms in order to develop a genetic map, determining if a plant carries the gene for a particular trait, determining the copy number of a particular gene in a plant, or for other purposes."

First, the precise identity of the nucleic acid molecules used in Dr. Wiegand's work is unclear. As stated above, we are limiting our consideration of the issues raised in this appeal as they pertain to the precise 469 nucleotide molecule set forth in SEQ ID No. 1. Dr. Wiegand's conclusions are premised upon use of "a nucleic acid molecule having the sequence of SEQ ID No. 1." It is unclear whether the probes used contained only the specific 469 nucleotides depicted in SEQ ID No. 1 or contained

additional nucleotides before and/or after the specific 469 nucleotide molecule set forth in SEQ ID No. 1.

In any case, it is not clear how the results reported in the declaration establish a substantial utility. Dr. Wiegand does not state in his declaration that these results provide any significant knowledge. To the contrary, they appear to represent what one might reasonably assume--a given EST may or may not detect a polymorphism in a related organism. While such knowledge may indicate the molecule is "useful" to some degree, we do not find that it represents a substantial utility.⁷

b. Probes or source of primers

Appellants argue that the specification "discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms...." Appeal Brief, page 16. While that may be true, it begs the question of what substantial use such knowledge would have? Again, the present specification does not attribute any property in terms of plant trait, or phenotype to the 469

⁷ We are aware that the examiner and appellants have engaged in a discussion on this record as to whether the specific soybean plants used in Dr. Wiegand's work are species and thus, whether the work is relevant in determining the utility issue. However, the manner in which the examiner and appellants have raised this issue in the context of this appeal proceeding does not provide a reasonable basis for its review. As stated by appellants, the issue was raised in an Advisory Action. Appeal Brief, page 15. Appellants responded to the assertions made in the Advisory Action by relying upon a dictionary definition in the Appeal Brief. The examiner discusses this portion of the Appeal Brief on pages 34-35 of the Examiner's Answer, stating that the cited dictionary reference was not provided and could not be evaluated by the examiner. The examiner then goes on to cite two other documents in support of his position. Appellants did not file a Reply Brief.

An appeal should be contested upon a fixed record, not upon an ever expanding and shifting record as here. It does not appear that appellants made the requisite showing under 37 CFR § 1.195 in presenting new evidence in conjunction with this appeal nor is it apparent that the examiner had authority to rely upon new evidence in support of his position. Under these circumstances, we decline to consider the issue.

nucleotide molecule of SEQ ID No. 1. Why does knowledge that a similar molecule may exist in another organism represent a substantial utility?

The same analysis holds for the stated utility that a nucleic acid molecule may be used in a "chromosome walk." Id., pages 16-17. In presenting this argument, appellants run afoul of the confusion engendered as to the source of the present nucleic acid molecules. Appellants' argument at page 17 of the Appeal Brief is couched in terms of the ability to isolate a promoter that is active in young seed pods (5 to 15 days after flowering). It appears that this argument is premised upon the fact that the nucleic acid molecule of the present invention was obtained from young seed pods. However, as explained above, the examples of the specification state that the nucleic acid molecule was obtained from young seeds collected from young pods.

Appellants state that the examiner denigrated the "chromosome walk" utility by stating in the Final Rejection that "[a]ny nucleic acid molecule from any plant cell generally serves this purpose...." Appeal Brief, page 16. Appellants argue in essence that despite the fact that the argued utility applies to all ESTs, there is no legal requirement that an invention's utility be "unique" to the invention, i.e., an invention can be a member of a class, where all the members of the class share a common utility.

First, appellants have only been required to identify a utility that is specific to the invention claimed. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695 (An invention does not have utility sufficient to satisfy § 101 until it is "refined and developed" to the point of providing a specific benefit in currently available form.). An invention certainly can have a utility that is shared by other compounds or compositions. Take, for

example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful as analgesics. On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

Nor does Dr. Wiegand's declaration assist appellants in this portion of their position on appeal. Dr. Wiegand discusses the use of EST's to generate probes in paragraphs 14-17 of his declaration. However, that work is based upon a synthetic probe stated to be "a true enough copy of SEQ ID No. 1." It is not apparent why evidence based upon "a true enough copy" of SEQ ID No. 1 is relevant in this appeal.

c. Other Arguments⁸

Appellants argue that the specification describes other utilities for the claimed nucleic acid molecules including "introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for compounds such as a herbicide." Appeal Brief, page 10. Specifically, appellants argue that a compound can be provided to both an antisense plant and a control plant not having antisense, with the effect of the compound on the plant being monitored. Appellants analogize this proposed procedure to a "cell-based assay" which appellants assert to have a "legally sufficient utility." Id.

Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. The portion of the specification cited in support of this argument (page 64) indicates that the nucleic acid molecule must be introduced into a plant cell and transcribed using an appropriate promoter to result in the co-suppression of an endogenous protein. The specification does not indicate that such a method is feasible when the nucleic acid to be used is uncharacterized as here. Such a use does not provide a specific or substantial benefit in currently available form.

⁸ Appellants present arguments in the Appeal Brief responding to issues apparently raised by the examiner previously but not maintained in the statement of rejection in the Examiner's Answer. For example, appellants argue that the examiner was incorrect as characterizing the claimed nucleic acid molecules as "tools" in the Final Office Action and Advisory Action. Appeal Brief, pages 11-12. However, the examiner does not characterize the claimed nucleic acid molecules in that manner in stating the utility rejection on pages 4-7 of the Examiner's Answer. Appellants also present arguments on pages 23-26 of the Appeal Brief in regard to whether the claimed nucleic acid molecules correspond to a pseudogene or are an artifact. However, in presenting his position on appeal the examiner does not rely upon either theory in stating the rejection, Examiner's Answer, pages 4-7. Apparently, the examiner no longer relies upon these rationales. Thus, we need not consider these issues.

Appellants also argue that the claimed nucleic acids are useful to measure the level of mRNA in a sample through use of microarray technology and use as molecular markers. Appeal Brief, pages 10-11. In regard to microarrays, appellants argue that it is "standard practice" to screen populations of nucleic acids with EST sequences without characterizing each and every target mRNA. Reference to para. 14 of the Wiegand declaration is made in support. Appeal Brief, page 11, n. 5. Dr Wiegand states "Soybean DNA clones are routinely used to detect expression levels of corresponding naturally occurring soybean nucleic acids. A nucleic acid molecule of SEQ ID NO: 1 can also certainly be used to detect expression level. Use of a nucleic acid molecule representing an EST as an expression probe is a practical use because it enables the detection of changes in expression of a particular gene." Wiegand decl., para. 14.

We find that the asserted utility of the claimed nucleic acid—as one component of an assay for monitoring gene expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form.

We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid depicted in SEQ ID NO: 1. However, the specification provides no guidance which would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification simply provides no guidance regarding what the SEQ ID NO: 1-specific information derived from a gene expression experiment would mean.

Suppose, for example, that a researcher found that SEQ ID NO: 1 expression was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. Maybe the meaning in a change in SEQ ID NO: 1 expression would depend on other factors, but again the specification provides no hint what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), the degree of increase? The specification simply provides no guidance as to how to interpret the results that might be seen using SEQ ID NO: 1 in a gene expression assay.

In effect, appellants' position is that the claimed nucleic acids are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the present case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, because even if used in gene expression assays, the

specification does not disclose how to use SEQ ID NO: 1-specific gene expression data.

Here, appellants assert that SEQ ID NO: 1, along with every other expressed soybean gene or protein, or for that matter, any expressed gene or protein, can be used to monitor changes in gene expression. However, without additional information, any observed results of changed expression of SEQ ID NO: 1 would have no meaning. The specification in effect discloses that the claimed nucleic acids can be used to monitor gene expression, and those of skill in the art will figure out what to do with the gene expression data. This utility is not substantial; it does not provide a specific benefit in currently available form.

Assuming arguendo that a generic gene expression assay—one based on monitoring expression of thousands of uncharacterized nucleic acids would provide a useful tool for, e.g., drug discovery, it does not follow that each one of the nucleic acids represented in the assay individually has patentable utility. Although each nucleic acid in the assay contributes to the data generated by the assay overall, the contribution of a single nucleic acid—its data point—is only a tiny contribution to the overall picture. The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently

available form. Providing a single data point among thousands or millions, even if the thousands or millions of data points collectively are useful, does not meet this standard. The Supreme Court noted that the patent system contemplates a basic quid pro quo: in exchange for the legal right to exclude others from his invention for a period of time, an inventor discloses his invention to the public. See Brenner, 383 U.S. at 534, 148 USPQ at 695. The Brenner Court held that the grant of patent rights to an applicant is justified only by disclosure of an invention with substantial utility – a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the applicant has not met his side of the bargain, and has not provided a disclosure sufficient to justify a grant of the right to exclude others. See id.

We reach the same conclusion in regard to appellants assertion that the nucleic acid depicted in SEQ ID NO: 1 is useful as a molecular marker or probe. It is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of SEQ ID NO: 1 as a molecular marker or probe represents a substantial use.

Appellants argue that ESTs have real world value as seen from the “growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs.” Appeal Brief, pages 19-21. Reliance is placed on paragraph 6 of the Wiegand declaration in support of this argument. Dr. Wiegand statements in this paragraph of his declaration refer to EST databases, clone sets and microarrays. Suffice it to say, the claims on appeal are not directed to EST databases, clone sets and/or microarrays. Again, it is not seen that the one data point which may be provided by using the

uncharacterized nucleic acid of SEQ ID NO: 1 in such devices represents a substantial use.

2. Enablement

There are two rationales set forth in the Examiner's Answer for this rejection. First, claims 1-3 are considered to be non-enabled "since the claimed invention is not supported by either a specific asserted utility or a well established utility for the set forth [in support of the § 101 rejection]. one skilled in the art clearly would not know how to use the claimed invention." Examiner's Answer, page 7. The examiner's second position focuses on claims 1 and 3 and their use of the transitional phrases "comprising" and "consisting essentially."

In regard to the first rationale, it appears that the rejection is simply a corollary of the finding of lack of utility. Thus, our conclusion with respect to the § 101 issue will also apply to this aspect of the § 112 (enablement) issue.⁹ On this basis we affirm the enablement rejection.

3. Written description

Only claims 1 and 3 are rejected under this section of the statute. The examiner has concluded that the use of the transitional phrases "comprising" and "consisting essentially of" in these claims results in appellants claiming an "astronomically large

⁹ Under these circumstances we need not reach the examiner's second rationale. However, we point out that the second rationale is premised upon an erroneous claim construction, i.e., the transitional phrases "comprising" and "consisting essentially of" are equivalent. If prosecution is resumed on this subject matter, the examiner should revisit the issue and construe "comprising" and "consisting essentially of" consistent with their well defined meanings. Also, as noted previously, the examiner did not make of record a fact-based analysis of the Wands factors. We urge the examiner in making any future enablement rejection, the rejection include an explicit analysis of the Wands factors.

genus of nucleic acid molecules" which are not "adequately describe[d]" by SEQ ID NO:

1. Examiner's Answer, page 10.

We do not find that this issue is ripe for review at this time and therefore decline to reach the merits of this rejection. The Appeal Brief was filed on January 31, 2001 and the Examiner's Answer was entered on August 6, 2001. Prior to the briefing in this appeal, the USPTO issued "Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, ¶ 1 "Written Description" Requirement, 66 Fed. Reg. 1099 (Jan. 5, 2001) (Guidelines). Neither appellants nor the examiner discussed the Guidelines and determined what affect, if any, they may have on their respective positions. In addition, the Federal Circuit has recently considered written description issues involving claims directed to nucleotide sequences and their use in hybridization assays in Enzo Biochem, Inc. v. Gen-Probe, Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002).

We believe a reasoned review of this rejection can only be performed after appellants and the examiner have had an opportunity to review the Guidelines and the court's opinion in Enzo. Since our affirmance of the utility rejection and the enablement rejection to the extent it is a corollary of the utility rejection constitutes a disposition of the appeal, we see no reason to remand the case for consideration of this issue now. Rather, if prosecution is resumed in this case, appellants and the examiner should revisit the issue and take into account the Guidelines and the guidance provided in Enzo.

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APPENDIX

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